A FORENSIC REVIEW AND EVALUATION OF THE REGULATORY AND ETHICAL FRAMEWORK GOVERNING HEALTH-RELATED RESEARCH IN POST-EBOLA LIBERIA

KOKULO FRANKLIN (M. Phil)
Student number: 217075678

SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF SOCIAL SCIENCE IN HEALTH RESEARCH ETHICS IN THE SCHOOL OF APPLIED HUMAN SCIENCES AT THE UNIVERSITY OF KWAZULU-NATAL, PIETERMARITZBURG, REPUBLIC OF SOUTH AFRICA

Supervisor:
Prof. Nhlanhla Mkhize

February 18, 2021

DECLARATION

I do hereby declare that the report, contained herein, is a true account of a work done by me under supervision, except where other sources have been duly acknowledged by means of references. Henceforth, I am solely responsible for any errors in this work.

[redacted]

Kokulo Franklin
Candidate

Date: February 18, 2021

I hereby declare that I did supervise the student in conducting the study contained herein, and do confirm that the student has my unreserved permission to submit it for assessment.

[redacted]

Prof. Nhlanhla Mkhize
Supervisor

Date: March 5, 2021

DEDICATION

This work is dedicated to the loving memories of my late mothers, Mother Kolu L. Dono and Mother Garmai Kolu Mulbah; and to the entire Franklin family, especially my darling wife Dr. Patience Dono Franklin, and our beloved children Garmai, Kokulo, and James.

ACKNOWLEDGEMENTS

First and foremost, I would like to say how grateful I am to the Almighty God for watching over me during my entire SARETI journey, a journey that was a very challenging experience, health-wise. Without HIM, all my efforts would have counted for naught.

Second, I would like to acknowledge the insightful supervision I received from my supervisor, Prof. Nhlanhla Mkhize. His experience and guidance proved to be absolutely immense, during the entire stages of this project, and it would have been literally impossible without him.

Third, my unquantifiable thanks and appreciations to my parents, Mr & Mrs David K. Franklin, and all of my siblings. Particular thanks go to my wife, Dr. Patience Dono Franklin, along with our children for guaranteeing my emotional stability. I am also grateful to my late Mother, Garmai Kolu Mulbah for her incessant sacrifice and prayers.

Special thanks also go to my employers, the Partnership for Research on Vaccines and Infectious Diseases in Liberia (PREVAIL), for giving me the utmost support in seeing me through this endeavour. The chance to take time off work and make use of their facilities in carrying out this project has been utterly invaluable. Some of my colleagues at PREVAIL, Mr. Moses Badio, Mrs. Marnijina M. Shannon, and Mrs Sienneh Z. Tamba, among others, were also very instrumental in my completion of this work, and to them, I remain eternally grateful.

Finally, I must register my sincerest heart-felt thanks and appreciations to Prof. Douglas Wassenaar, Ms Carla Pettit (Mama SARETI), the experienced Facilitators, and the entire family of the South African Research Ethics Training Initiative (SARETI) for this life-changing opportunity.

ABSTRACT

BACKGROUND

The end of the deadly 2014 Ebola outbreak in Liberia has seen a noticeable influx of western researchers into the country. Given the vulnerable nature of the majority of Liberians (impoverished and poorly educated), this raises a lot of ethical concerns. This study sought to gauge the local research governance frameworks to discover what protective structures and documented stipulations exist, since there has never been any such assessment.

METHODOLOGY

The study made use of a triangulated qualitative design, involving a desk review of fifteen (15) national guidelines, policies, procedures, and regulations, coupled with eleven (11) in-depth key informant interviews with purposively-identified oversight institutions and some researchers.

RESULTS

Key documents (Public Health Law, National Research for Health Policy, and the Clinical Trial Guidelines, National Research Ethics Board Guidelines, and the University of Liberia – Pacific Institute for Research and Evaluation IRB Handbook), along with key institutions (Ministry of Health, the National Public Health Institute of Liberia, the Liberia Medicines and Health Products Regulatory Authority, the National Research Ethics Board, and the University of Liberia – Pacific Institute for Research and Evaluation (UL-PIRE) IRB) were found to be critical to the overall governance, review, approval, and monitoring of health research in Liberia. The frameworks governing health research were found to contain most of the traditional protective stipulations, though significant gaps were also identified from the desk review and in-depth interview with the major stakeholders. Stipulations on emerging issues (stored samples, bio-banks, genetic/genomic research, and data ownership and sharing) and contextually relevant issues (post-trial access, ancillary care, and consent in local languages) are evidently absent or only fleetingly mentioned.

CONCLUSION

Overall, Liberia appears to have in place the relevant foundational frameworks for acceptable governance of health research. However, the documents are in need of substantial overhaul and contextualisation, especially given the rapidity with which legal and ethical governance of health research has advanced over the past few decades. The local institutional governance is also in need of reorganisation, something that will enhance adequate coordination and management of health research.

Table of Contents

List of Tables

List of Figures

CHAPTER 1

INTRODUCTION

This chapter presents a panoramic overview of the pivotal issue of the national ethical and legal governance of health research, and briefly touches on the specific problem that the study sought to address, i.e. the particular situation with research governance in Liberia. It also includes the clearly stated objectives of the study, definition of some of the key words, and a concise illustration of what the exact scope of the study is.

1.1 Background

Though the contributions of health research to the advancement of human civilization is immeasurably immense, it is not without some significant drawbacks, especially in relation to the use of humans as the subjects of scientific investigation. The involvement of humans in the conduct of health research always throws up a binary dilemma between scientific interest and individual rights (Katz, Capron, & Glass, 1972). Essentially, the crux of the issue is the extent to which the need to understand and remedy diseased conditions can be allowed to outweigh the rights and safety concerns of human participants of health research. Historically, this issue has proven to be a very difficult balancing act for the scientific community. The gruesome nature of the Nazi experiments, the Pfizer Meningitis trial, and the Tuskegee Syphilis Study are usually cited as instances where the quest for knowledge on human conditions had descended into outright barbarity (Amdur, 2011; Huijstee & Schipper, 2011; Nwabueze, 2016; Okonta, 2014).

To curtail the likely recurrence of such egregious acts, there have been concerted efforts to promulgate international guidelines and laws meant to address this scar on the consciousness of the entire scientific community. As a consequence of this drive, there are now many guidelines and regulations by which to hold accountable researchers and medical practitioners. Some of these include the oft-cited Nuremburg Code, Council for International Organizations of Medical Sciences (CIOMS), Belmont Report, and the Declaration of Helsinki (CIOMS, 2016; National Commission, 1979; Office for Human Research Protections, 2010; The Nuremberg Code, 1948; World Medical Association, 2013).

These attempts at the international regulation of health research, while unquestionably laudable, have a couple of challenges: (1) as guidelines, they are non-binding; and (2) because they are meant to be general in scope, they might be in need of adaptation to fit prevailing contexts of different places. As a consequence of this 'non-binding' nature of these guidelines, for example, different institutions or countries around the world could possibly choose when and how to follow them. To illustrate this point, the Nuremburg Code (1948), Declaration of Geneva (1948), and the first Declaration of Helsinki (1964)

were all in existence when some of the earlier cited research abuses were carried out. The fact that some of these guidelines were in existence did not bind those researchers, because there was nothing in their local jurisdictions obliging them to follow the stipulations of these guidelines. By themselves, these guidelines are almost entirely aspirational and, where there are no nationally accepted regulatory frameworks, would be left to the whims and caprices of researchers, as alluded to by Nichols (2016).

In light of these realities, there has been a determination, on the part of many nations and organisations, to advocate for and put in place nationally relevant legal and ethical benchmarks to govern health research (Andanda, 2010; CIOMS, 2016; Grant, Lewis, & Strode, 2005; Kirigia, Ota, Motari, Bataringaya, & Mouhouelo, 2015; Office for Human Research Protections, 2018; Sombié, Aidam, & Montorzi, 2017; Strode, Slack, & Mushariwa, 2005; Walanj, 2014). These national instruments, in principle, are meant to ensure that the stipulations espoused in the cited guidelines are no longer just aspirational desires to do what is right, but that they have an enforceable element that would require all involved in the conduct of health research in those respective jurisdictions to comply (Andanda et al., 2011; Nuffield Council on Bioethics, 2002).

This critical need for context-specific regulation of health research is even more relevant now, given the noticeable increase in the "pace and scope" of international collaborative research between low- and middle-income countries (LMICs) and wealthy countries of the developed world (Nwabueze, 2016). A typical fact in such countries is that there are usually many vulnerable populations, something that is further compounded by the fact that they also have very weak regulatory infrastructures, making them susceptible to exploitation by unscrupulous researchers (Bishop, 1995; Tegli, 2018; Washington, 2007).

Despite this urgent relevance, there are accounts that in terms of the institution of context-specific regulations and mechanisms, a number of LMICs, especially those on the African continent, are in a less than optimal state (Ndebele, Mwaluko, Kruger, Ouwe Missi Oukem-Boyer, & Zimba, 2014; Ndomondo-Sigonda, Miot, Naidoo, Dodoo, & Kaale, 2017; Office for Human Research Protections, 2018; Sombié et al., 2017). These reports present a mixed picture. Whereas some countries like South Africa have fairly well-structured and defined regulations and mechanisms, others like Guinea-Bissau are apparently lagging behind.

Another country whose situation has been seemingly unsatisfactory, or in need of a degree of clarity, is the West African state of Liberia, where the research governance system has been described as being poorly coordinated (Ministry of Health, 2018). The issue of what context-specific protective provisions exist, or indeed the general health research governance set-up, has been in dire need of clarity, especially given the influx of researchers from western countries, in the immediate aftermath of the 2014 Ebola crises. It is only with such "clarity" – the motivating centrepiece of this current study – that an understanding of what protections are currently guaranteed, or indeed what protective stipulations or mechanisms are needed, can be fully appreciated in the country.

1.2 Aims and Objectives

The aim of this study was to determine the regulatory and ethical framework governing health related research in Liberia

1.3 Specific Objectives

In terms of specifics, the study set out to:

1. To determine the ethical-legal frameworks that are governing health research in Liberia.
2. To assess the specific protections for research participants that are guaranteed therein.
3. To find out the institutions/structures involved in the review, approval, and monitoring of health research.
4. To explore the perspectives and experiences of key stakeholders – like the ministry of health, ethics and regulatory authorities, and current or former researchers – on the governance of health research in Liberia.
5. To proffer meaningful recommendations to improve the system, where needed.

1.4 Synopsis of Methodology

To have successfully achieved the stated aim and objectives, this study made use of a methodological triangulation, involving a review of available relevant national documents, along with an in-depth interview with major stakeholders involved with the governance and conduct of health research in Liberia.

1.5 Delimitation of the Study

The prime focus of this study was to get an insight into the status quo, *vis-à-vis* the pivotal issue of the governance of human participant research in Liberia, by carrying out a baseline audit of the nature and content of the research governance framework existing in the country. Though the audit was coupled with an interview with key stakeholders, this was meant to get a practical sense of the frameworks, *vis-à-vis* their perceived strengths and weaknesses, as experienced by these stakeholders. Its focus was not to render a definitive verdict as to the preparedness of the local system to provide the protections needed.

1.6 Key Words and Abbreviations

Below is a list of some key words and abbreviations used in this study:

National Regulatory Frameworks: Refers to the institutional and documentary or policy frameworks governing health research in Liberia

Institutional Framework: Refers to the list of institutions that are collectively overseeing the governance of health research in Liberia

Documentary/Policy Framework: Refers to the collection of documents (regulatory & ethical) that are being used to govern health research in Liberia

Emanuel et al. Framework: The eight (8) principles proposed by (Emanuel et al., 2004) for the ethical conduct of research in low-resource settings

Liberia: The West African nation at the centre of this study

LMHRA: Liberia Medicines and Health Products Regulatory Authority

NREB: National Research Ethics Board

NPHIL: National Public Health Institute

MoH: The Liberian Ministry of Health

UL-PIRE: University of Liberia – Pacific Institute for Research and Evaluation

NHRC: National Health Research Council (proposed)

CIOMS: Council for International Organizations of Medical Sciences

1.7 Conclusion

This chapter introduced the issues of health research and the need for its regulation, the lack of clarity in Liberia, and what this study is meant to achieve.

CHAPTER 2

LITERATURE REVIEW

This chapter centres on a review of the available literature on the subject of governance for research involving human participants. It includes a brief look at the essence of health research, presents instances where the research enterprise has gone astray and attempts that have been made to prevent same, including summaries of some major international guidelines. It also contains a critical assessment of the body of work that has been done in this area from the continental, regional, and sub-regional levels, and finally proceeds to make the case for delving into the case of Liberia, by laying bare the critical lack of clarity in the country. The specific questions guiding said investigation are also included.

2.1 Significance of Health Research

Centuries of medical research and clinical practice have led to phenomenal successes and breakthroughs that have had far-reaching impacts on the quality of life of millions of populations world-wide. As pointed out by Das and Sil (2017), medical research has provided information trends and risk factors of diseases, and enabled humanity to develop innovative interventions that have saved and improved the quality of life for millions of people. Many diseases like malaria, meningitis, polio, HIV and AIDS, and smallpox could not have been relatively contained, or in some cases completely eradicated (Hinman, 1998), had it not been for the scientific curiosity and meticulous research work of the scientific community. The ongoing attempts to find a workable vaccine for the 2014 Ebola virus disease outbreak that ravaged West Africa (Agnandji et al., 2016; Ledgerwood et al., 2017; Tangwa, Browne, & Schroeder, 2018) is a prime example of how research has been used over the centuries to address health challenges faced by global populations

2.2 The Dark Side of Medical Research

As apparently glorious as the gains made by medical research have been, there have also been some dark chapters in this pursuit of "generalizable knowledge". A review of the history of medical research involving the use of human beings as subjects of scientific inquiry, throws up quite a number of examples of how, in the name of understanding or finding a cure for diseases, some unscrupulous scientists have engaged in activities that border on outright cruelty. From James Lind using sailors for a scurvy experiment to Edward Jenner's use of children for a smallpox experiment, or Guiseppe Sanarelli's controversial yellow fever investigation, history contains numerous examples of investigators blatantly violating the rights of human participants (Emanuel et al., 2003; Jenner, 1800;

Krans, 2013; Lind, Stewart, & Guthrie, 1772; Sade, 2003). A number of widely publicised examples of such research violations are presented below.

2.2.1 International Cases

Two of the most notorious examples of research abuse include the ghastly Nazi Experiments on prisoners and the Tuskegee Syphilis Trials. The Nazi experiments rank high amongst the worst cases of scientific malpractice ever reported. As cited by Gomes (2010), these experiments were conveniently divided into three (3) categories: military, pharmaceutical, and racially influenced experiments. Specifically, the experiments included transplants of bones, muscles and nerves; sterilisation; high-altitude experiments, where prisoners were placed in environments to observe how long they could last without oxygen; freezing experiments, in which prisoners were forced to remain in extreme cold or made to bath with freezing water for hours; deliberate infection with malaria and Typhus, in order to test various possible treatments; and seawater experiments (BestPsychologyDegrees, 2018; Gomes, 2010; Spitz, 2005). These horrific and debilitating "experiments" reportedly resulted in death or permanent impairments, with more than 15,000 cases having been documented (Weindling, von Villiez, Loewenau, & Farron, 2016).

For the Tuskegee Study, a 40-year nontherapeutic study done in the south of the United States, between the years 1932 to 1972 (Amdur, 2011; Jones, 2008), similar cruelty was recorded Conducted by an arm of the federal government, the study involved 600 poor, uneducated blacks (400 with syphilis – the experimental group; and 200 without Syphilis – the control group). The stated purpose of the study was to investigate and record study the effects of untreated syphilis. The researchers also intended to get data from this all-black study to compare with an all-white study referred to as the Oslo Study (Clark & Danbolt, 1955; Jones, 2008). A decision was made by researchers to withhold any sort of treatment from all study participants, so that even when penicillin became available as an effective treatment for this devastating disease, it was withheld, as patient after patient succumbed to their sickness. Their bodies were then used for further observations.

2.2.2 Violations from the African Continent

Africa, as a continent with a large number of poorly-educated and economically-deprived populations, coupled with the fact that most countries on the continent have very weak and, in some cases, non-existent regulatory infrastructure (Howell & Obado-Joel, 2016; Ndebele, Blanchard-Horan, Shahkolahi, & Sanne, 2014; Nwabueze, 2016), has not been spared, when it comes to scientific malpractice. As extensively outlined by Ndebele, Mwaluko, et al. (2014), the relatively short history of biomedical

research on the continent has recorded some horrific abuses, ranging from the notorious case of the British doctor in Zimbabwe, who illegally carried out medical investigations on about 500 patients, mostly black, some of whom actually died as a result of his actions; the unapproved Pfizer trial, on about 200 children, of an experimental meningitis drug in the west African state of Nigeria, which tragically resulted in deaths and other debilitating effects; or indeed the widely-referenced actions of the discredited South African oncologist, Dr. Werner Bezwoda.

2.3 Drive Towards International Regulation

Disregarding the time of occurrence, these violations exposed the critical need to erect, where lacking, or strengthen, guardrails along the busy highway of human research, especially as it pertained to the acquiescence of study participants. Though the Nuremburg trial, along with its resultant ethical code, is famously regarded as the starting point for research regulation, especially on the issue of the consent of participants, there are many accounts that some publications and practices long predated Nuremburg (Beecher, 1970; Sade, 2003; Weindling, 2001; Weindling et al., 2016). However, the symbolism of having research scientists on trial for wrongful deeds sent out a very powerful message to the scientific community, and the resultant code of medical ethics, the Nuremburg Code, though rudimentary in scope, laid the foundation for a number of the international guidelines (Fischer, 2006). In these guiding documents, there is, generally, a very clear attempt at defining the allowable contours of research involving humans. The fact that one of the defences put forward by the Nazi doctors during their trial was the absence of standing ethical conventions that they could have referenced (Emanuel et al., 2003) made this drive at international regulation an urgent imperative Few of these guiding documents are elaborated on below, though they are by no means the only ones.

2.3.1 Nuremburg Code

The Nuremburg Code is one of the most historic and often quoted documents in the field of human participant protections. When it was produced, it represented a monumental break from the past, where research endeavours involving human participants were conducted with little or no regard to their rights and welfare. The Code is presented in ten (10) different points, each outlining conditions that must be met before humans can be used for research purposes. Perhaps the most significant of the ten points is the first one which unequivocally declares that “the voluntary consent of the human subject is absolutely essential”. The Code requires that for a consent to be valid, the person concerned must have full legal capacity to consent, be under no pressure to do so by external parties, and have the necessary information key to his decision. Among other significant stipulations of the Code, the study must be

conducted by qualified individuals, have a favourable risk-benefit/risk-knowledge analysis, and guarantee a right of withdrawal from the study. Given that it has not been revised since its publication, the document is silent on a number of pertinent ethical concerns, for example community engagement/participation, post-trial access, or even ancillary care.

2.3.2 Helsinki Declaration

The Helsinki Declaration was first released in 1964 by the World Medical Association (WMA). Since then, it has been revised more than eight (8) times, most recently in 2013. The latest version (2013) has been hailed for responding to contemporary research issues, especially in resource-limited settings (Ndebele, 2013).

The declaration has some important requirements or benchmarks, including voluntary informed consent, prior knowledge, scientific and social value, favourable risk-benefit or risk-knowledge ratio, and be conducted by qualified individuals (academically and ethically). It also requires the submission and approval for research protocols before initiation of trials, assent when dealing with individuals who cannot legally consent (like children), recommends post-trial provision of products of research, insists on a plan for providing compensation for participants, in case of research-related injuries, and requires that research studies are publicly registered and that they are obliged to publish or disseminate research findings, whether positive or not.

2.3.3 Belmont Report

The Belmont Report is segmented into three (3) parts: Section A covers the distinction between medical practice and research; Section B outlines the three (3) ethical principles of respect for persons (that the autonomous nature of each individual is respected, and that those with limited autonomy be given special protection), beneficence (that everything is done to maximise the benefits and minimise the harm for research participants), and justice (that there are genuine efforts to fairly distribute the burdens and benefits of research); and Section C sets forth the different practical applications of principles (that respect for persons underpins Informed Consent, that beneficence underlies the risk-benefit or risk-knowledge analysis, and that justice supports the fair selection of research participants).

2.3.4 CIOMS

Established in 1949, the Council for International Organizations of Medical Sciences (CIOMS) was asked by the WHO to translate the first version of the Helsinki Declaration into a working document that would serve as a guide for member countries of the WHO (Fischer, 2006). Consequently, the first version of the CIOMS guidelines was released in 1982. Since then, there have been about four (4) revisions: 1993, 2002, 2009, and the latest version in 2016. Segmented into about twenty-five (25) guidelines, CIOMS also contains two pertinent appendices, one for the different items that should be included in health-related study protocol, and the other about the different pieces of information that should be covered in the informed consent process. Summaries of some of the guidelines' major stipulations are given in Appendix 11.

2.3.5 45 CFR 46

This document presents a set of guidelines to guide the conduct of research involving human participants, especially those studies that are being funded by the America Government (Fischer, 2006). In 1981, the Department of Health and Human Services (DHHS) and the Food and Drug Administration (FDA) issued Codes of Federal Regulations (CFRs), Title 45 Part 46 and Title 21 Parts 50 & 56, respectively (University of Missouri-Kansas City, 2017). Ten (10) years later, the DHHS regulations (45 CFR 46), particularly subpart A, were adopted by about sixteen (16) other Departments of the Federal Government, thereby leading to this code being referred to as the "Common Rule" (Fischer, 2006). The full constituent subparts of 45 CFR 46 are subparts A, B, C, D, & E (Office for Human Research Protections, 2010). The different subparts of 45 CFR 46 have their own emphasis and were added to or modified at different times. Summaries of some of the code's major stipulations are given in Appendix 12.

2.3.6 Other Complimentary Documents

Generally, all of the above guidelines try to clearly outline the acceptable conditions under which biomedical research involving humans can proceed. Interestingly, at about the same time that most of these bioethical documents were being formulated, and probably as a response to the outrage surrounding some of the earlier-cited research violations, there were also attempts, by world organisations like the United Nations and other relevant international institutions, at developing some additional and complimentary documents by which nations could be held liable, especially regarding human rights, fundamental freedoms and human dignity of all peoples across the globe (Office of the

United Nations High Commissioner for Human Rights, 1976; UNESCO, 2005; United Nations, 1949, 1989). These documents unequivocally outline that each individual, regardless of which part of the world he or she is resident in, what language he or she speaks, or what he or she looks like, has some basic human rights that must always be provided for and respected. These humanitarian documents usually provide another layer of protection for research participants, and in countries where there are no clearly laid out ethical-legal regulations in place for the protection of potential and actual research participants, citizens in those countries, especially if their countries are signatories to these international humanitarian documents, can lay credible claims to the protections that are espoused in these documents.

2.4 Attempt at Harmonisation of Documents

In view of the aforementioned, there is no paucity of international documents (bioethical or human-rights-based) that are purportedly meant to streamline the conduct of research involving humans. One concern raised with bioethics, however, is that, in some instances, there may be a preponderance of different documents, to the extent that this could cause confusion as to which documents to use and when (Macklin, 2005). This state of affairs may have given rise to the desire to establish harmonised documents, drawing from different sources that could somehow help to ameliorate the obfuscation. This quoted as one of the reasons for the development of the ICH-GCP document (International Council for Harmonisation (ICH), 2016), especially as it relates to clinical trials.

Another example is the seminal work of Emanuel et al. (2004), which has tried to bring some degree of ethical order. In terms of guidelines, the work stipulates, based on a careful review of major international bioethical documents, some features of what would constitute ethically acceptable clinical research, especially in LMICs, where resources are often very limited and ethical and regulatory infrastructures are weak or non-existent. Essentially, the Emanuel et al. framework is presented as eight (8) well-articulated principles (see Appendix 10), which are carefully and systematically broken down into thirty-one (31) very specific benchmarks which serve to tick the key boxes. Though the framework is not without legitimate criticisms, and the authors are first to accept (as laid out in the paper), it has turned out to be a very useful tool for ethicists globally.

2.5 Enforcement Mechanisms

Without a workable framework to ensure the implementation and enforcement of their stipulations, all of the many guiding documents that have been presented here would have amounted to nothing. Perhaps this was the reason why the architects of the drive to regulate the conduct of research with humans had

found a way of framing structures and systems to serve as recognisable guardrails on the potentially perilous highway of medical research. Some of these structural ethical checkpoints include ethics committees, and medicine or drug regulatory authorities.

2.5.1 Research Ethics Committees (RECs)

Though not described in some of the earlier international guiding documents, it is now perhaps inarguable to say that the role IRBs play in contemporary research processes is the most critical (Bhat & Hegde, 2006). An ethics committee serves mainly as an entity that focuses on "what is right or wrong and on what is desirable or undesirable", as it relates to protecting the rights and welfare of research subjects (Amdur, 2011). There are two types of research ethics committees: independent ethics committees, which are usually independent of any particular institution or entities; or institutional review boards, which are usually set up by a host institution and serve the purpose of internal review. Regardless of the configuration, this should not affect their core function as outlined, as they must be composed of competent individuals and be independent in their evaluation of protocols (Woodin, 2011). Different international guidelines contain carefully-crafted stipulations regarding the setting-up, membership, procedures, and detailed functions of ethics committees (CIOMS, 2016; Office for Human Research Protections, 2010).

2.5.2 Drug and Other Regulatory Authorities

Working in close concert with ethics committees are other governmental institutions or agencies that have oversight responsibilities for health research, especially in the case of clinical trials (Grant et al., 2005; Office for Human Research Protections, 2018). These regulatory agencies have laws and other policies that could have implications for research, and as such research institutions or individual investigators must always be aware of and ensure compliance with such laws. Additionally, especially in the case of drug authorities, their roles also apply to the review, approval, and post-approval market surveillance of drugs. In Africa, it has been reported that though drug and other regulatory agencies or authorities are present in almost all countries, their capacity is extremely poor and their ability to carry out their regulatory functions is severely compromised (Nayyar et al., 2015; Ndomondo-Sigonda et al., 2017).

2.6 Unsatisfactory State of Research Regulation in Africa

Though there has been noticeable spread of the culture of institutionalising and nationalising ethical and regulatory requirements for the conduct of health-related research, some countries seem to be ahead of others (Ndebele, Mwaluko et al., 2014; Office for Human Research Protections, 2018), with a series of reports suggesting notable inconsistencies across the continent (Andanda et al., 2011; de Vries et al., 2017; IJsselmuiden, Marais, Wassenaar, & Mokgatla-Moipolai, 2012; Kirigia et al., 2015; Mbondji et al., 2014; Ndebele, Mwaluko et al., 2014; Sombié, Aidam, Konaté, Somé, & Kambou, 2013; Sombié et al., 2017). While countries like South Africa, Zimbabwe, and Nigeria have tried to institute nationally relevant frameworks, policies, and guidelines to protect their citizens who are potential or actual participants in health research, other countries on the continent, it appears, might still be lagging behind (Andanda et al., 2011; de Vries et al., 2017; Ndebele, Mwaluko et al., 2014; Ogunrin, Daniel, & Ansa, 2016; Strode, Slack, & Essack, 2010; Strode et al., 2005).

In a large-scale continent-wide survey to assess the state of national health research systems (NHRS) of forty-six (46) countries located in the WHO's African region, a number of interesting general findings were reported (Mbondji et al., 2014). On the whole, the study concluded that research systems in these 46 countries (a number that roughly accounts for over 80% of the Continent's nation states) were largely "weak". This wide-ranging study found that only 36% of countries surveyed reported having a functional national research governance mechanism. Moreover, as critically important as ethics committees are to the contemporary health research process (Amdur, 2011; Bhat & Hegde, 2006; Nichols, 2016), this survey found that about 25% of those surveyed didn't have functional ethical review committees. On the question of having a "law relating to health research", of the 40 countries that responded, only a modest 17% responded in the affirmative. Astonishingly, it was also found that, at the time, there were some countries (four in all), with no ethical or scientific regulatory bodies at all.

A very similar study to the aforementioned painted a slightly brighter picture of things across the continent (Kirigia et al., 2015). This study, which involved 47 countries in the same WHO African region, found that between 2003 and 2014, the percentage of countries with a functional national health research system increased from 30% to slightly above 50%. Other interesting findings were that 49% of the countries surveyed had a national health research policy; 40% of them reportedly had legislation governing research, as opposed to the 17% reported by Mbondji et al. (2014); and that about 47% reportedly had budget lines for research. This study also reported that only a meagre 9% of the countries reported not having functional ethical review committees, a vast difference from the 25% reported by Mbondji et al. (2014). Despite this seemingly positive report, the study concludes that despite the progress some countries had made at improving some of their NHRS, there "remains an urgent need for countries without NHRS to establish them and for others to improve the functionality and efficiency of every NHRS component" (p. 1).

A number of studies have also been done to assess the status quo in some countries across the continent. Earlier in this decade, an audit of ethical and legal frameworks in the five (5) Western, Eastern, and Central African countries of Cameroon, Malawi, Nigeria, Rwanda, and Zambia also gave a glimpse of how some countries on the continent fare in this regard (Andanda et al., 2011). For instance, while all these countries reportedly had some "statutory and administrative" entities with the "capacity" to legally and ethically regulate health research, idiosyncratic differences were also reported, both structurally and functionally. All of the countries, except Zambia, were reported, for example, to have national Research Ethics Committees, though in some (Malawi and Rwanda) this body reviews and approves research, and in others (Cameroon and Nigeria), these bodies "oversee, register, and regulate ethics committees". On the cardinal issue of post-approval monitoring of research, the audit found that Zambia and Cameroon had no mechanisms to effect this, while Nigeria, Rwanda, and Malawi did have infrastructure to carry out post-approval monitoring. This is a problem in most African countries (Nyika et al., 2009). Encouragingly, some countries, like Malawi and Rwanda in this study, have ethical guarantees enshrined into their national constitutions. These two countries have a clearly spelt out requirement for "informed consent" in their constitutions, while in Nigeria, the National Health Bill guarantees the right to informed consent. The other countries involved in this study have generic references to general human right provisions like rights to "personal liberties", and "right not to be tortured or treated inhumanely". On the issue of post-trial access, another report (Andanda, Gxoyiya, & Mahenge, 2010) found that this was still a very huge challenge in these countries.

In the ECOWAS region, where Liberia is located, a study to evaluate the general state of research for health infrastructure at the Ministries of Health concluded that there was urgent need for action to improve the research environment in these countries (Sombié et al., 2013). While 85% of the countries in this study reportedly had broader national health research policies, only 50% of them had established directories for health research with defined terms of reference. According to the same report, support for research structures and the building of research capacity is being hamstrung by the inadequacy of funds. In line with the findings from this report, a 2017 paper on efforts to strengthen national health research systems in the four (4) West African countries of Guinea-Bissau, Sierra Leone, Mali, and Liberia, also stressed the need for long-term engagement in order to deal with challenges and strengthen health research systems in these countries (Sombié et al., 2017).

2.7 Lack of Clarity in Liberia

About the West African state of Liberia, there exists very little record, as it relates to the governance frameworks, including the processes, structures, and policy guidelines or regulations, that are being utilised to streamline the conduct of health research. Whatever semblance of a governance structure that might be in existence also appears to be very poorly coordinated. As vividly captured in section 1.1 of the 2018 Research for Health Policy (RHP) (Ministry of Health, 2018), the prevailing situation has been characterised by the "lack of governance, coordination, and management". Quite shockingly, a recent report by Sombié et al. (2017) makes the claim, something that is supported by the RHP, that the country does not even have any budget line in the Ministry of Health budget in order to finance health research, which by extension would affect the institution and operationalisation of any regulatory structures and mechanisms.

Apart from this evident lack of clarity surrounding the structural or operational research governance system, there is also no record of there ever having been a systematic and methodical audit of the existent, hopefully context-specific, regulatory and ethical documents; neither has there ever been a recorded study of the perspectives of major stakeholders concerning the structural frameworks and protective stipulations contained or absent in these documents. Consequently, it is unclear the extent to which internationally accepted stipulations like the mandate for ethics review, the requirement for informed consent, and the requirement for a favourable risk-benefit ratio, the necessity of community involvement in the development and implementation of protocols, or indeed post-trial access to beneficial interventions, are provided for in local ethical and regulatory instruments.

2.8 Rationale of the Current Study

This unclear state of affairs is profoundly problematic, especially given the influx of researchers in the aftermath of the 2014 Ebola crisis. These mostly north-south collaborative research endeavours, which have an attendant history of exploitation of poor and underprivileged communities, some in Africa (Ahmad, 2001; Bishop, 1995; Parker & Kingori, 2016; Washington, 2007), have raised the ethical and legal stakes significantly. Moreover, the noticeable involvement of big pharmaceutical companies and, as a consequence, the introduction of the profit motive and its attendant ethical minefields (Okonta, 2014), has undoubtedly added another layer of significance and urgency to this problem. Concerns have rightly been expressed that, in the absence of nationally appropriate frameworks, especially those firmly grounded in key ethical principles, there is a strong likelihood of western researchers or research institutions taking advantage of this lax or fuzzy regulatory environment (Huijstee & Schipper, 2011; Ndebele, Mwaluko et al., 2014). As pointed out by Nwabueze (2016), it is probably due to such weak

or absent regulations or enforcement mechanisms that the notorious 1996 Pfizer trials in Nigeria, or indeed the case of the unscrupulous Zimbabwean doctor (Bishop, 1995), were possible.

Combined, these aforementioned problematic realities have served to provide the ultimate incentive for the immediate clarification of the prevailing situation in Liberia. The need for a thorough systematic audit of the existent local ethical and regulatory frameworks cannot be overemphasised. Such a forensic audit will, for the first time, provide a clear idea of the ethical and legal instruments and institutions that exist, along with a detailed delineation of the specific protective stipulations or guarantees that are provided for, or absent, in these instruments. It is only with such baseline audit of the system that a clear picture as to what is obtaining, or indeed, what needs to be done can be obtained. This research project sought to do that, by assessing what national ethical-legal structures and policies are in place in Liberia to properly ensure the protection and welfare of research participants. Such a complete review and evaluation is fundamental, moving forward.

2.8.1 Research Questions

In a bid to achieve this, the following questions have been formulated to guide this investigative endeavour:

1. What ethical-legal frameworks (guidelines, policies, procedures, regulations, and laws) are governing health research in Liberia?
2. What are the specific protections guaranteed in the framework governing health research in Liberia?
3. What institutions or structures are involved in the review, approval, and monitoring of health research?
4. What are the perspectives and experiences of key stakeholders – like the ministry of health, ethics and regulatory authorities, and current or former researchers – on the governance of health research in Liberia?
5. What meaningful recommendations can be made to improve the system, moving forward?

2.9 Conclusion

This chapter has laid out the importance of health research when it comes to the advancement of human civilisation, given a historical account of the issue of research violations and abuse, and pointed out past and current attempts to address the problem. It also presented summaries of key literature on the issue

of research governance on continental, regional, and sub-regional levels; continuing to illustrate the critical lack of clarity as to what is obtaining in the West African state of Liberia and the need to correct this.

CHAPTER 3

RESEARCH METHODOLOGY

This chapter deals with a detailed delineation of all of the methods and procedures that were followed to achieve the stated aims and objectives and provides clear answers to the stipulated research questions of the study. It gives the paradigmatic positioning of the study, describes the method triangulation used, spells out how the documents were assembled and stakeholders recruited, and details how the collected data were meticulously analysed. It also includes the ethical implications for conducting the study, along with what was done to address them.

3.1 Research Paradigm

This study was informed by an interpretivist philosophical persuasion, and was firmly grounded on the contents of the documents, along with the expressed views of the stakeholders consulted for the research. This was meant to allow for the interpretation of the text and interview transcripts, which represent the unique perspectives of these stakeholders, whether in the form of the words in the documents or the interview responses. As suggested by Kivunja and Kuyini (2017), meticulous care was taken to retain focus on, and give meaning to, the texts analysed, along with the views of respondents, and avoid introducing the views of the researcher.

3.2 Study Design

Strongly informed by this interpretivist paradigm, the study made use of a triangulated qualitative research design (*Figure 2*), which specifically involved documentary analysis of fifteen (15) national ethics and regulatory documents (laws, policies, procedures, and guidelines), coupled with semi-structured interviews with key stakeholders. Given the focus of this work, it was important to use this triangulated approach, as it provided the flexibility needed to not only audit the assembled documents, but also to gauge the practical and operational proficiency of the frameworks, by hearing directly from those involved with their formulation and enforcement, as well as those whose activities are meant to be streamlined by the frameworks. Additionally, this design also lent credibility to the findings and reduced biases (Bowen, 2009; Triad 3, 2016), as the two approaches ideally complemented each other. For example, concepts that were not clear in the documents were elucidated during the interviews and vice versa.

3.3 Study Location

This study was conducted in Liberia, a country situated on the coast of West Africa (*Figure 1*). Liberia has a current population of 4.7 million inhabitants (Worldometer, 2017), of which about 95% are African indigenous groups (16 tribal groups in all), with the rest mainly accounting for descendants of repatriated freed slaves from America and other parts of the world (World Population Review, 2017). As a typical low and middle income country (LMIC), it is one of the poorest and most under-developed countries in the world. According to the 2018 UNDP's human development report, the country is ranked 181 out of a total number of 189 nations in the world, with a Human Development Index (HDI) of 0.435 (UNDP, 2018).

Figure 1: *Map of Liberia* (*OnTheWorldMap*, *2018*)

Despite having a manageable population, in comparison with other West African countries, basic health and socio-economic indicators are mostly abysmal (African Health Observatory, 2014; Liberia Institute of Statistics and Geo-Information Services (LISGIS), 2014; Liberia Institute of Statistics and Geo-Information Services (LISGIS), 2009; National Malaria Control Program, 2012).

3.4 Study Population and Sampling

A total number of eleven (11) participants were recruited for this study (*Table 1*). This number included five (5) representatives (Reps) or contact persons (CPs) from key oversight institutions, along with six (6) current or former research scientists. The oversight institutions represented included the Liberian Ministry of Health (MoH), the Liberia Medicines and Health Products Regulatory Authority (LMHRA), the National Public Health Institute of Liberia (NPHIL), and two local ethics committees (National Research Ethics Board (NREB) and University of Liberia – Pacific Institute for Research and Evaluation Institutional Review Board (UL-PIRE IRB)).

For the interviews, a purposive sampling method was utilised to pre-select the aforementioned five (5) oversight entities (MoH, NPHIL, LMHRA, NREB, and UL-PIRE IRB). The heads of entities were contacted, and asked to identify and recommend knowledgeable individuals from their entities to serve as the CPs. Furthermore, a mass email was sent to a list of active and former researchers, some associated with prominent local research entities, about twelve (12) in all. The first six (6) to express an interest and sign the consent were recruited as part the study, while the remaining six (6) where excluded solely based on their late or no response. A purposive sampling method was deemed to be the most preferable for this study because the study specifically aimed to interview only individuals deemed to be integral to the governance, reviewing, approving, conduct, and monitoring of health research in Liberia.

In the case of the desk review, the identification of the targeted ethical-legal documents was done through two principal tracks (*Figure 2*). Firstly, there was a broad online search, especially of well-known international databases like the International Compilation of Human Research Protections, country-specific Training and Resources in Research Ethics Evaluation (TRREE) compilations, Health Research Web (HR Web), and the ClinRegs platform. Particularly, search terms or phrases like "research in Liberia", "governance of health research in Liberia", "clinical research in Liberia", "research ethics committees in Liberia", "African health systems research", "health research documents in Liberia", "constitution of Liberia", "health systems regulation in Africa", and "ClinRegs Liberia" were used to cast as wide a search net as possible, so as to get enough documents for the documentary analysis. Secondly, key informants were also relied upon to suggest additional sources of information or relevant documents that might not have fallen into the online search net.

Table 1: *Summary Information of Interviewees*

Interviewees	
Participants/Institutions	**Number**
LMHRA	1
NREB	1
UL-PIRE	1
NPHIL	1
MINISTRY OF HEALTH	1
PRACTITIONERS/RESEARCHERS	6
TOTAL	**11**

3.5 Methods

3.5.1 Desk Review

For the purpose of this study, the fifteen (15) documents that were reviewed included national, ethics committee, and regulatory documents (laws, policies, procedures, and guidelines). Specifically, these documents included the Constitution of the Republic, the guidelines of the National Research Ethics Board (NREB), Handbook of the University of Liberia - Pacific Institute for Research and Evaluation IRB (UL-PIRE IRB), the clinical trials guidelines and the Act creating the Liberia Medicines and Health Products Regulatory Authority (LMHRA), amongst others (*Table 2*).

3.5.2 Key Informant Interviews

As pointed out above, a total of eleven (11) key informants representing key oversight institutions were interviewed. Using a semi-structured interview format, these major stakeholders were interviewed for their knowledge and experiences of, and roles in, the current ethical-legal frameworks being used to regulate health research activities. Views as to what improvements are needed were also sought. Interview schedules (Appendices 3–7) were shared with the CPs and researchers, in advance of the scheduled interviews, so as to allow for consultation or information gathering, where necessary. Conducting these interviews was critical because, as pointed out by (Bowen, 2009), documents are not always conclusive or accurate. It was therefore meant to get a more practical overview of whatever framework is in existence. On average, interviews lasted for about 37 minutes each.

3.6 Data Analysis

Using Content Analysis, the targeted documents were coded and thematically interpreted using steps and guides as described by various accounts (Bowen, 2009; Centers for Disease Control and Prevention, 2009; O'Leary, 2014; Triad 3, 2016). These steps also proved helpful, especially when it came to becoming familiar with the assembled documents. The documents were specifically evaluated to assess the different levels of protections that are stipulated or absent in them, especially with regards to the participant protections that are enshrined in the latest versions of internationally recognised guidelines like the Nuremburg Code, Declaration of Helsinki, Belmont Report, 45 CFR 46, CIOMS, and ICH-GCP.

However, as these various international guidelines all have their differences, a structured evaluation of the collected ethical and legal documents was done by using a document assessment framework (DAF) (Appendix 8). This DAF was developed by modifying the benchmarks in the Emanuel et al. framework (Emanuel et al., 2004). It was designed to pay particular attention to whether there are unambiguous provisions for contextually relevant ethical issues like social responsiveness, community participation at different stages of the research cycle, protections for vulnerable populations, fair selection of participants, compensation for research-related injury, post-trial access, and ancillary care. In order to tease out which of these cardinal ethical benchmarks are addressed in the assembled ethical and legal/regulatory frameworks or documents, a Document Assessment Table (DAT) (Appendix 9) was used as a tool.

As for the key informant interviews with the major stakeholders, responses were thematically organised in categories that were in line with, and meant to answer, the specific research questions earlier outlined. These responses were gleaned to discover the latent or manifest thematic contents (Boyatzis, 1998; Braun & Clarke, 2006; Clarke & Braun, 2013; Joffe, 2012). An in-depth and meticulous manual analysis approach, utilising different features of Microsoft Word (including highlighting and commenting) and Microsoft Excel was used to perform the coding and identify pertinent themes (Belotto, 2018). To give some context and meaning to these responses, reasonable interpretations were provided (Joffe & Yardley, 2004). While the preconceived perspectives that shaped the research questions were at the forefront, there was a deliberate attempt to pick up on inherent thematic perspectives that emerged from the data (Boyatzis, 1998; Joffe, 2012).

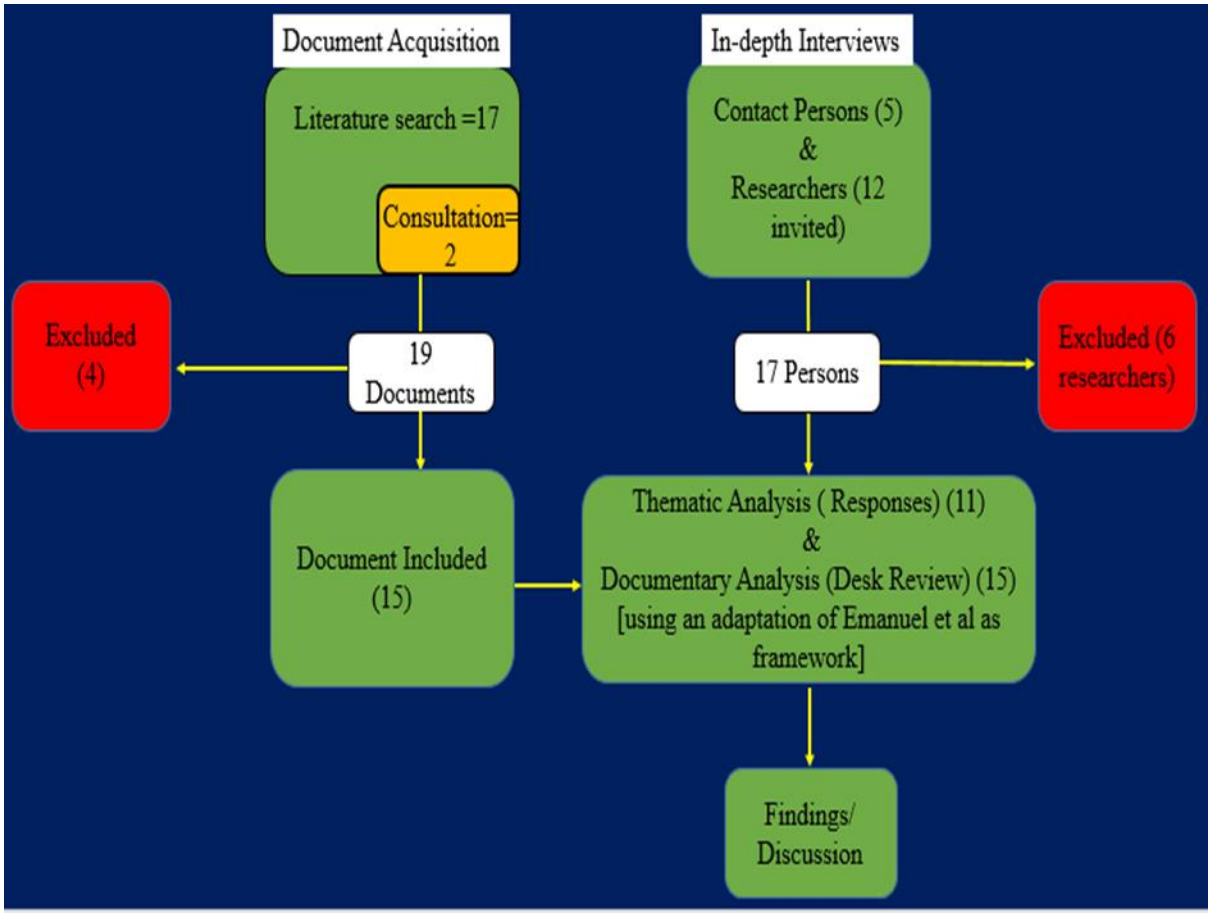

Figure 2: *Flow of Research Activities*

3.7 Credibility/Trustworthiness

To ensure that data collected and analysed by this study were credible, a number of deliberate steps were taken during the conduct of the study. Perhaps the most important of these was the decision to employ the triangulated qualitative design (Tobin & Begley, 2004). According to a number of sources, triangulation has been reported to serve as a way of adding rigor and deepening understanding of topics under consideration (Carter, Bryant-Lukosius, DiCenso, Blythe, & Neville, 2014; Golafshani, 2003; Patton, 1999; Tobin & Begley, 2004). Specifically, this study made use of method triangulation, as described elsewhere (Carter et al., 2014; Polit & Beck, 2012). This involved the coupling of rigorous review of pertinent ethical and legal documents with an in-depth interview of stakeholders, perspectives from whom, added context and clarity where lacking in the review. Though no method is flawless, the use of this combined method provided a degree of credibility and trustworthiness.

Additional strategies employed to ensure the trustworthiness of the data and the results reached from them were those of "prolonged engagement" and "member check", two strategies effectively described by Korstjens and Moser (2018). In this study, "prolonged engagement" refers to the prolonged time

spent with the documents that were assembled for review. Essentially, between five (5) to six (6) months were spent reading through these documents, so as to ensure total familiarity with them, something that made the arduous processes of coding and thematic categorisation a lot easier. In total, all the key documents, including the interview transcripts were carefully read through at least three (3) times. As it relates to the "member check" strategy, it alludes to the numerous post-interview instances where interviewees were repeatedly contacted during the transcription and coding of the data, to ensure that views were accurately represented, in addition to seeking clarifications where needed.

3.8 Ethical Considerations

3.8.1 Community Participation

For the purpose and scope of this study, there was no need for mounting a typical community engagement outreach, as it mainly involved review of literature, with only a handful of key informants that were recruited through purposive sampling arrangement. However, given that interviews were done with representatives from institutions (MoH, LMHRA, NPHIL, and ethics committees), gatekeeper permissions were solicited and obtained (all but one) from these institutions (Appendices 17–20).

3.8.2 Social and Scientific Value

This study fulfilled the requirements of ensuring social and scientific value. The issue of ethical and legal protection for human participants of health research, especially in a resource-limited settings like Liberia, is a very pertinent one. Hitherto, there has been no documented assessment of existent ethical-legal frameworks in Liberia, something that is essential, in order to lay the basis for possible plans to rectify any potential lapses. This study aimed to do that. The methodological design of a desk review of relevant documents and semi-structured interview of relevant stakeholders aptly provided answers to the study questions. In addition, the study was conducted by a combined investigator-supervisor team with relevant academic and ethics training.

3.8.3 Ethics Review

As with all research involving human participants, which must be approved by an appropriately constituted ethics committee, this study was reviewed and approved by the University of KwaZulu-Natal Biomedical Research Ethics Committee (BREC) (approval #: BE401/18; Appendix 21) and the

University of Liberia – Pacific Institute for Research and Evaluation IRB (UL-PIRE IRB) (approval #: 18-08-122; Appendix 22), in South Africa and Liberia, respectively.

3.8.4 Favourable Risk-Benefit/Risk-Knowledge Ratio

The study was designed to have a favourable risk-benefit ratio. There was no direct risk to the participants or their institutions, and the knowledge accrued from the successful completion of the study will provide in-depth insight as to the status quo, when it comes to research participant protection in Liberia**.** This could possibly be useful to the entire country, in terms of correcting any potential lapses in the ethical-legal safety net for current and future participants of health research. Additionally, participants were given $ 10.00 USD, as an appreciation for taking time away from their work schedules.

3.8.5 Informed Consent

Individuals who were contacted to participate in the interviews were provided sufficient information about the study (see sample of Information Sheet – Appendix 1) and asked to provide informed consent (see sample of Informed Consent – Appendix 2) before being interviewed and recorded, in keeping with international best practices in health research. They were explicitly informed that their participation was completely voluntary, and that they could opt out of the interview at any time of their choosing. Clear efforts were made to ensure that no interviewee was being pressured to represent their entity against their will. Probably because of the fact that the interviewees were all conversant with the tenets of human participant research, there were no notable challenges with the consenting process.

3.8.6 Fair Participant Selection

The participants of the study were mainly representatives of selected institutions, who are major stakeholders in the conduct of health research in Liberia; a handful of researchers were also engaged. They were asked to participate because they are best positioned to provide great insight, as it relates to the governance of health research in Liberia.

3.8.7 Continuing Respect

All efforts were made to ensure that the confidentiality of participants was protected during and after the study. Interviews were done at a place and time of the participants' choosing, in addition to the use of appropriate pseudonyms for each interviewee. Anonymised recordings and data from the interviews will be kept in a secure locker for five (5) years, after which they will be appropriately discarded.

Additionally, as one reason for doing this study was to help further the discourse around protections for health research participants, findings from the study will be shared with participating entities and relevant authorities, both through direct delivery of copies and presentations at local scientific fora. The ultimate hope, especially in keeping with the requirement for social value, is that these findings will be used to improve or make policy, or serve as basis for advocacy.

3.9 Conclusion

This chapter gave a holistic presentation of the paradigmatic underpinnings of this study, including a description of the methodological steps taken to delve into and answer the key research questions that were being investigated. It illustrated the strong ethical foundation of the study, and also spelled out the steps that were taken to ensure that the study's findings are trustworthy and credible.

CHAPTER 4

RESULTS

This chapter deals with the presentation of the specific findings or results of the study. In terms of specifics, results show that the documentary framework governing health research in Liberia includes, the Public Health Law, National Research for Health Policy, the Clinical Trial Guidelines, National Research Ethics Board Guidelines, and the University of Liberia – Pacific Institute for Research and Evaluation IRB Handbook. Interestingly, these documents were found to contain most of the traditional protective requirements (informed consent, ethics review, favourable risk-benefit ratio, etc), though significant gaps – stipulations on emerging issues (stored samples, bio-banks, genetic/genomic research, and data ownership and sharing) and contextually relevant issues (post-trial access, ancillary care, and consent in local languages) – were also identified from the desk review and in-depth interviews with the major stakeholders. It was also established that in terms of institutional governance, key institutions like the Ministry of Health, the National Public Health Institute of Liberia, the Liberia Medicines and Health Products Regulatory Authority, the National Research Ethics Board, and the University of Liberia – Pacific Institute for Research and Evaluation (UL-PIRE) IRB) are critical to the overall governance, review, approval, and monitoring of health research in Liberia, though these institutions also have serious human resource, logistic, and financial constraints. This inadequate nature of the structural and functional components of the local research governance apparatus is something that was also stressed by the major stakeholders interviewed for this study.

These results, which include those from the content analysis performed on the assembled documents, coupled with stakeholders' (contact persons of the oversight entities and the researchers) perspectives on a range of important research ethics and governance issues, are presented in accordance with the order of the specific research questions, as laid out earlier. Additionally, appropriate tables, graphs, and quotes from the respondents, were used to illustrate the key findings.

4.1 What are the Ethical and Legal Documents Governing Health Research in Liberia?

The study set out to determine the main ethical and legal documents currently being used to govern the conduct of health research in Liberia. To this, the results from the interviews with the stakeholders (*Figure 3*) and the review of the documents (*Figure 4*) point to five (5) major governance documents. For convenience, these documents are sorted into two major categories, namely: 1) regulatory or legal documents (Public Health Law (PHL), National Research for Health Policy (RHP), and the Clinical Trial Guidelines (CTG)) which, for the purpose of this work, loosely refer to all those guidelines,

policies, and laws of the Liberian government; and 2) ethics documents (National Research Ethics Board (NREB) Guidelines and the University of Liberia – Pacific Institute for Research and Evaluation (UL-PIRE) IRB Handbook), which refer to guidance documents from those local ethics committees or institutional review boards. In addition to these major documents, other local documents that were found to have relevant stipulations are presented in *Table 2*.

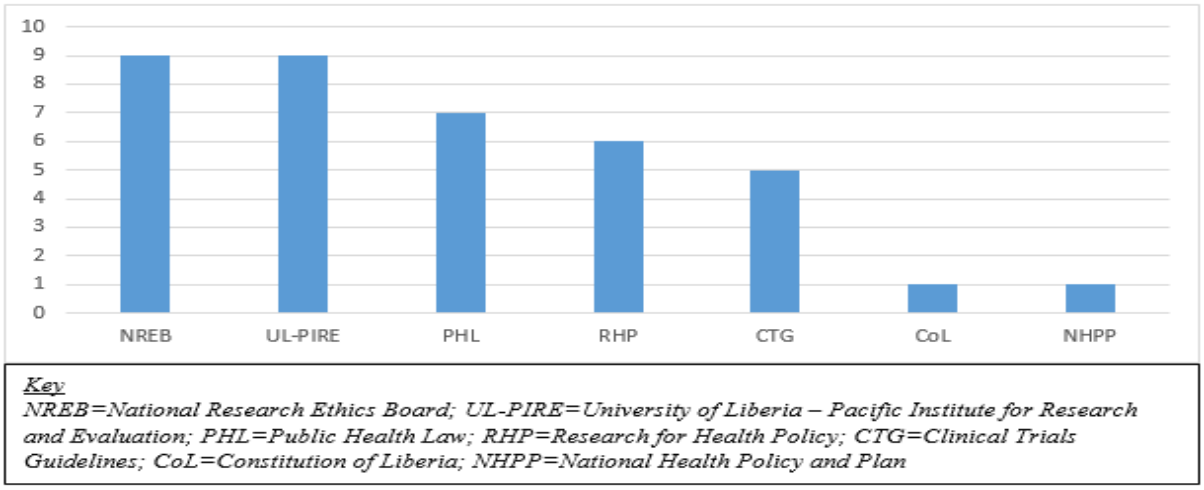

Figure 3: *Key Research Governance Documents according to interviewees*

Table 2: *Different Documents Analysed*

Documents	Entities	Years of Publication
Constitution of Liberia (*CoL*)	National/Justice Ministry	**1986**
Children Law	Ministry of Gender, Children and Social Protection	**2011**
National Child Welfare and Protection Policy (*CWP*)		**2017**
Clinical Trial Guidelines (*CTG*)	Liberia Medicines and Health Products Regulatory Authority (LMHRA)	**2014**
Medicines & Health Products Regulatory Authority (*LMHRA*) *Act*		**2010**
Penal Code	National/Justice Ministry	**1978**
National Research for Health Policy and Strategy (*RHP*)	Ministry of Health (MoH)/NPHIL	**2018**
National Health and Social Welfare Policy and Plan 2011–2021 (*NHPP*)		**2011**
National Health Communication Strategy (*NHCS*)		**2016**
Public Health Law Title 33 Liberian Code of Laws Revised (*PHL*)		**1976**
National Public Health Institute of Liberia Act (*NPHIL Act*)		**2017**
Human Right Act	National Human Rights Commission	**2005**
Liberia Institute of Statistics and Geo-Information Services Act (*LISGIS Act*)	LISGIS	**2004**
National Research Ethics Board (*NREB*) *Guidelines*	NREB	**2014**
University of Liberia – Pacific Institute for Research and Evaluation (*UL-PIRE*) *IRB Handbook*	UL-PIRE	**2008**

4.2 What are the Specific Protections for Research Participants spelled out in the Local Documents?

Another objective of the current study was to review and analyse the contents of local documents to note the specific protective stipulations that are contained in or absent from them. In addition to the five (5) major documents identified above, ten (10) other pertinent national laws and policies (*Table 2*) were meticulously analysed, as explained earlier. The results indicate that these documents have varying levels of important protective stipulations (*Figure 4*) and a total of 29 identified benchmarks from the documents. These benchmarks, the individual stipulations (quotations or summaries) associated with them, along with the exact locations of the stipulations in the cited documents, are presented under the appropriate Emanuel et al. Principles (*Tables 3 to 10*). Appendix 14 (blotted red) shows the seven (7) benchmarks that were absent from the assembled documents.

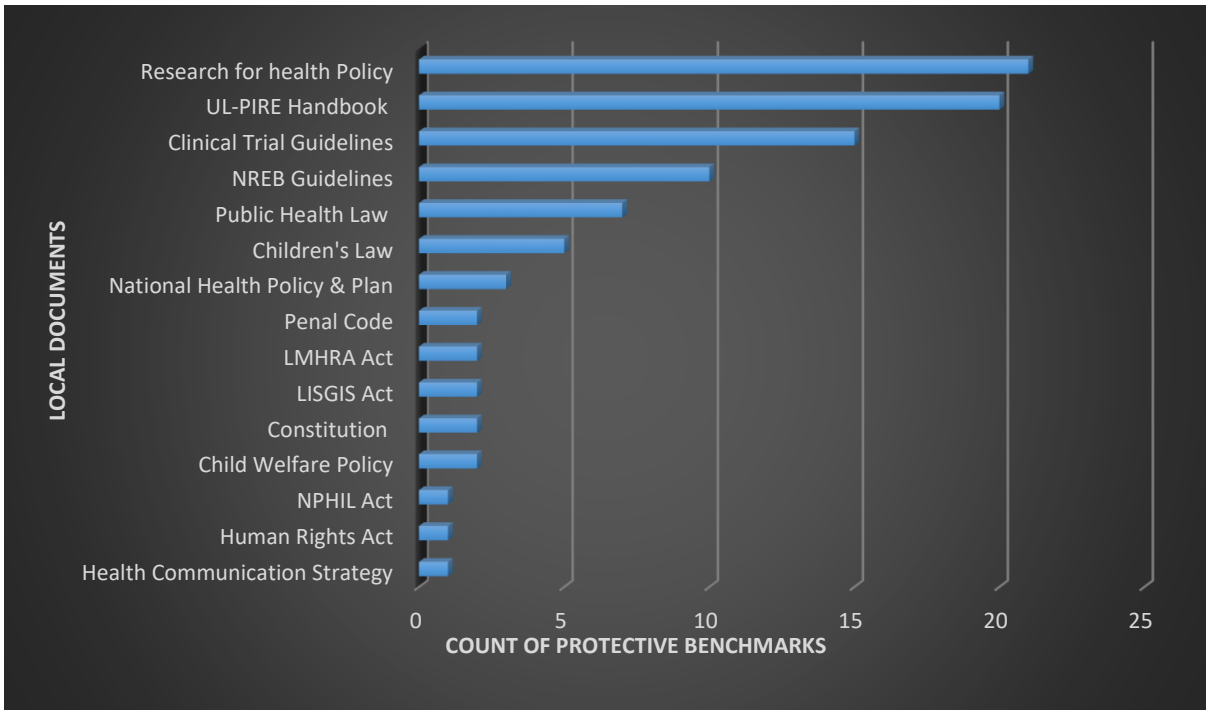

Figure 4: *Local Documents with Protective Stipulations*

4.2.1 Principle 1: Collaborative Partnership

Table 3 displays, under the Emanuel et al. principle of collaborative partnership, the four (4) key protective or ethical benchmarks found in the local ethics and regulatory documents that were assessed. These include: promotion of fair collaborative research partnerships, need for community involvement and synergic interactions with local authorities, requirement for capacity building, and requirement to comply with local laws/regulatory compliance. These key provisions are contained, per the analysis, in the following documents: the Research for Health Policy, the National Health Policy & Plan, the

LMHRA Act, the National Health Communication Strategy, the Public Health Law, and the Clinical Trials Guidelines of the LMHRA.

Table 3: *Protective/Ethical Stipulations in Local Documents*: *Collaborative Partnership*

Emanuel et al. Principle	Protective/Ethical Benchmarks	Source (s)	
		Document(s)	**Specific stipulation(s) & location(s)**
Collaborative Partnership	*Promotion of fair collaborative research partnerships*	Research for Health Policy	**Section 2.1.2:** highlights the one-sided nature of international collaborative partnerships **Section 3.2.6:** MoH shall "promote strategic partnerships with public and private research institutions and a cross-section of other stakeholders"
	Need for community involvement and synergic interactions with local authorities	Research for Health Policy	**Annex 2:** researchers to clearly state the extent of "user involvement in design of the study" **Section 3.2.3:** partners and conductors of research to "effectively communicate" their research activities to the public in a "timely and relevant manner"
		National Health Policy & Plan	**Section 4.15:** "third parties" to consult the MoH on "all matters" when it comes to health and social welfare research
		LMHRA Act	**Part 5 section 6:** prohibition on the advertisement and promotion of medicines & health products in a misleading way; authority shall review said materials
		National Health Communication Strategy	**Section 3.1:** "communication interventions and messages will be coordinated and harmonized so all partners speak with one voice" p. 24 **Section 4.5:** require approval of health related messages by the MoH
		Public Health Law	**Sections 18.12 & 18.13 of Part II:** discourage dissemination of false, misleading, or unapproved messages, especially about HIV/AIDS
	Requirement for Capacity building	Research for Health Policy	**Section 2.3:** "Liberia's future research development and growth depends largely on human and physical capacities" **&** **Section 4.3:** need to build capacity of researchers to "conceptualize, conduct, analyse, disseminate, and translate research for health data"
		Clinical Trials Guidelines	**Section 2.9:** need for capacity building plan, when applying for approval

	Requirement to comply with local laws/regulatory compliance	Research for Health Policy	**Section 3.2.5.3:** research carried out in Liberia to be conducted in keeping with "all relevant Liberian laws, national policies, regulations and guidelines (public health law, human right law, national health policy and plan) as well as in tandem with international law" **Annex 2:** researchers to state whether they have received regulatory approval

4.2.2 Principle 2: Social Validity

As presented in *Table 4*, three (3) key protective or ethical stipulations under the principle of social validity, namely, the need to prioritise and address local health needs, the requirement for results publication/dissemination and utilisation, and the need to prevent the weakening of local systems, were noted from the analysis of the local documents. Under this principle, the Research for Health Policy, the Clinical Trials Guidelines, and the UL-PIRE Handbook contained pertinent provisions.

Table 4: *Protective/Ethical Stipulations in Local Documents*: *Social Validity*

Emanuel et al. Principle	**Protective/Ethical Benchmarks**	**Source (s)**	
		Document(s)	**Specific stipulation(s) & location(s)**
Social Validity	*Need to Prioritise and address local health needs*	Research for Health Policy	**Section 3.2.1:** MoH prioritises "research and innovation relevant to meeting health priorities and promoting development and equity at all levels of the health system" **Section 3.2.4:** stakeholders conducting research in the country to prioritise health needs of the country
	Results publication/dissemination and utilisation requirement	Clinical Trials Guidelines	**Section 4.14:** researchers to include, in their application package, a clear "publication policy"
		Research for Health Policy	**Annex 2:** researchers to clearly state whether or not they "intend to publish or present" their findings **Section 2.4:** establishment database to "capture all protocols submitted to the institutional review boards (IRB) and research results" **Section 2.4.1:** plans for a series of scientific gatherings to bring together researchers and policy makers to share and discuss research findings and to have these findings making their way into national policies

		UL-PIRE Handbook	**Part VI subpart I (2 (f)):** researchers to indicate "how and with whom the results will be shared"
	Prevent weakening of local system	Research for Health Policy	**Annex 2:** researchers to clearly outline the "resource implications to the host organization and any other involved departments" of their research activities

4.2.3 Principle 3: Scientific Validity

This study found, as exhibited in *Table 5*, three (3) key protective or ethical stipulations under the principle of scientific validity. These include: the requirement for qualified and experienced investigators (local investigator for multinational studies), the requirement for clear and justified methodology, and the requirement of prior knowledge. Under this principle of scientific validity, pertinent local documents included: Public Health Law, Clinical Trials Guidelines, NREB Guidelines, UL-PIRE Handbook, and the Research for Health Policy.

Table 5: *Protective/Ethical Stipulations in Local Documents*: *Scientific Validity*

Emanuel et al. Principle	**Protective/Ethical Benchmarks**	**Source (s)**	
		Document(s)	**Specific stipulation(s) & location(s)**
Scientific Validity	*Requirement for qualified and experienced investigators*; *local investigator* (*multinational studies*)	Public Health Law	**Section 61.2 of part 7:** need to register and license all medical and allied health professionals
		Clinical Trials Guidelines	**Section 2.16:** need for curriculum vitae of investigator(s) **Section 3.2 (p. 10):** appropriate university degree and requisite experience **Section 3.3:** need for a national investigator for multisite trials **Section 3.4:** requirement for "formal training in Good Clinical and Laboratory Practices (GCLP) within the last two years"
		NREB Guidelines	**Section 2.8:** research should be "closely supervised by a person or team with experience, qualifications, and competence appropriate to the research"
		UL-PIRE Handbook	**Part VI subpart D, paragraph 5 (p. 19):** Investigator has ultimate responsibility for acceptable ethical research
	Requirement for clear and justified methodology	Research for Health Policy	**Annex 2:** full explanation on the use of particular methodological approaches, including randomisation methods that will be used; use appropriate study designs that will answer the research questions
		Clinical Trials Guidelines	**Section 4:** requirement for a clearly described trial design

		NREB Guidelines	**Section 2.8:** requires that the "design and methodology of the research is appropriate to achieving desired aims"
		UL-PIRE Handbook	**Part VI subpart A (2) (a)–(h):** provide details on the procedures that will be used for the study
	Requirement of prior knowledge	Research for Health Policy	**Annex 2:** investigators of proposed studies must have done sufficient review of existent literature
		UL-PIRE Handbook	**Part VIII subpart A:** investigators of proposed studies must have done sufficient review of existent literature
		Clinical Trials Guidelines	**Section 4.2:** requires the presentation of preclinical findings, reference literatures, and data that are relevant to the proposed study

4.2.4 Principle 4: Fair Selection of Participants

As presented in *Table 6*, there are three (3) key protective or ethical benchmarks under the principle of fair selection of participants, as found in the local documents examined. These include: requirement for fair and equitable selection, contain clear definition for vulnerable persons, requirement to ensure protection for vulnerable persons. Under the current principle, the following local documents were found to contain pertinent provisions: Research for Health Policy, Clinical Trials Guidelines, UL-PIRE Handbook, NREB Guidelines, Children's Law, and Child Welfare Policy.

Table 6: *Protective/Ethical Stipulations in Local Documents*: *Fair Selection of Participants*

Emanuel et al. Principle	**Protective/Ethical Benchmarks**	**Source (s)**	
		Document(s)	**Specific stipulation(s) & location(s)**
Fair Selection of Participants	*Requirement for fair and equitable selection*	Research for Health Policy	**Annex 2:** concise description of the participant population, along with the justification for using that particular population
		Clinical Trials Guidelines	**Section 4.5:** delineation for the criteria for the selection; fair basis for selection of research participants
		UL-PIRE Handbook	**Part VI subpart G:** require fairness in the selection of research participants and research generally
		NREB Guidelines	**Section 2.1:** fairness in the selection of research participants and research
	Contain clear definition for vulnerable persons	Clinical Trials Guidelines	**Section 1.2:** definition of vulnerable populations
		UL-PIRE Handbook	**Part VI subpart G:** definition of vulnerable populations
		Children's Law	**Article 7 sections 1.1–1.2:** outline of situations that would constitute

			"vulnerability" and "special vulnerability" for children, including having no parent or guardian, having no home, among other situations
	Requirement to ensure protection for vulnerable persons	Research for Health Policy	**Section 3.2.5.2:** vulnerable populations: their rights and dignity "should be protected, according to the law of Liberia"
		Child Welfare Policy	**Section 2.4.1:** the responsibility for the protection of the rights of the child rests with all stakeholders concerned **Section 2.4.2:** stresses the "best interest" of the child, when it comes to the "interpretation and application" of the policy
		Children's Law	**Part 11 sections 3 & 13:** establishment of Child Welfare Committee and National Child Well-being Council, respectively
		UL-PIRE Handbook	**Part VI subpart G:** caution against enrolling for participants from vulnerable populations; need for protective provisions to guide against exploitation of such individuals or groups

4.2.5 Principle 5: Favourable Risk-Benefit Ratio

Under the Emanuel et al. principle of favourable risk-benefit ratio, this study categorised three (3) different ethical benchmarks or stipulations. As captured in *Table 7*, the relevant benchmarks include: requirement for favourable risk-benefit ratio, presence of clear definition for "risks" and "benefits", and provisions on handling research abuse or violation. Individual provisions making up these categorised benchmarks can be found in the following local ethical and regulatory documents: Research for Health Policy, Clinical Trials Guidelines, NREB Guidelines, UL-PIRE Handbook, National Health Policy & Plan, Public Health Law, LMHRA Act, and the Human Rights Act.

Table 7: *Protective/Ethical Stipulations in Local Documents*: *Favourable Risk-Benefit Ratio*

Emanuel et al. Principle	**Protective/Ethical Benchmarks**	**Source (s)**	
		Document(s)	**Specific stipulation(s) & location(s)**
Favourable Risk-Benefit Ratio	*Requirement for favourable risk-benefit ratio*	Research for Health Policy	**Annex 2:** researchers to "outline the methods by which the patient/subject's interests will be safeguarded. For example, the process of risk limitation"
		Clinical Trials Guidelines	**Appendix 9.3:** "before a trial is initiated, foreseeable risks and inconveniences must be weighed against the anticipated benefit for the individual trial study participant and society. A trial should be initiated and continued only if the anticipated benefits justify the risks" (p. 46)

		NREB Guidelines	**Section 2.1:** beneficence is one of the cardinal ethical values and principles to be considered, when conducting "human research in Liberia" **Section 2.8:** whatever benefit derived from a research should "outweigh any possible harm to participants."
		UL-PIRE Handbook	**Part VI subpart A (2 (a)–(h)):** ensure that all risks to the "safety, dignity, rights and welfare of the subjects" are compared with the potential benefits to the participants and the society at large
	Contain clear definition for "risks" and "benefits"	Research for Health Policy	**Section 2.5:** risk is "the probability of physical, psychological, social or economic harm or injury occurring because of participating in a research study"; risks can range from "minimal to significant" **Section 2.5:** benefit is "desired outcome or advantage for participating in a research study"
		UL-PIRE Handbook	**Part VI subpart B (5):** Definition for risk **Part VI subpart B (6):** "minimal risk" is risk "not greater, considering probability and magnitude, than those ordinarily encountered in daily life of that subject, or during the performance of routine physical or psychological examinations or tests" (p. 18) **Part VII subpart B:** different levels or categories of risk, including 'Level I', pose no risk to human participants; 'Level II', only minimal risk; while 'Level III', involves "possible risk" to participants, include vulnerable populations, or a sensitive topic. **Part VIII subpart B:** Definition of benefit
	Provisions on handling research abuse or violation	National Health Policy & Plan	**Section 6.3:** MoH to enforce PHL "in collaboration with judicial and police authorities", advise on "proper procedures for managing cases of professional misconduct", and to initiate public awareness programs on acceptable practices and those that are "forbidden by law", as well as "how to proceed when legal infringements are suspected"
		Public Health Law	**Part 7 section 61.5:** all licensed medical or allied health professional are subject "to the procedures and penalties for professional misconduct as prescribed" in the PHL **Part 7 section 61.21 (a)–(g):** outlines examples of professional misconduct: practicing on a suspended or expired licence, practising with incompetence or negligence, or allowing or aiding an unlicensed person to perform activities that require a licence

			Part 7 section 61.22: lays out what should happen when a charge is filed against a particular professional by an aggrieved party (person, corporation, association); first heard by professional board concerned, after which recommendations will be made to the Minister **Part 7 section 61.23:** punitive actions: minister can either exonerate or impose penalties like suspension, revocation, or limitation on renewal **Part 2 section 18.15:** (Interpretation): members of a research team who clumsily, recklessly, carelessly, or negligently infects another person is liable to prosecution, including the possibility of civil action
		LMHRA Act	**Part 4 section 2.1 (s):** LMHRA to "receive and investigate complaints regarding alleged violations of the Act or any regulations promulgated by the Authority, and impose appropriate sanctions in accordance with regulations promulgated by the Authority under this Act, and consistent with the Administrative Procedure Act of the Republic of Liberia and with due process of law" **Part 8 section 1:** number of administrative sanctions (confiscation, license or permit revocation, and financial penalties)**,** **Part 8 section 2:** additional civil penalties **Part 8 section 3:** additional criminal penalties; Between the civil liabilities and criminal penalties, "whichever act provides a greater length of imprisonment or higher fine" is preferred
		NREB Guidelines	**Section 1.12:** guidelines specifies that "research misconduct" will be addressed in keeping with their SOP, and that any misconduct that falls outside of the remit of the ethics committee guidelines "will be dealt with under governmental processes for dealing with other forms of misconduct" **Section 2.13:** stress the authority of the Board to withdraw an approval, if there are protocol or participants' rights violation **Section 2.7:** participants to be given information of contact, in the event they need to complain a researcher/research institution; "first instance of a complaint shall be directed to the NREB ethics committee"
		UL-PIRE Handbook	**Part VI subpart D, paragraph 1 (p. 19):** University's Director of research is responsible for "immediately reporting all

			research-related problems to the appropriate agencies and must work with the University of Liberia in communicating with government agencies with respect to addressing the necessary assurances and policies" **Part VIII subpart C:** participants to be given information of contact, in the event they need to complain a researcher/research institution
		Human Rights Act	**Article IV sections 1-3:** commission can "take up" cases of human rights violations, receive "complaints and petitions" directly from victims or other third parties, and can submit said to authorities, either by its own or at the request of said authorities **Article VI section 1 (a)–(f):** the commission can summon individuals accused of human rights violations because it has subpoena and other quasi-judicial powers **Article III section 2 (a)–(b):** international agreements to which Liberia is a party to can be invoked in appropriate circumstances

4.2.6 Principle 6: Independent Review

With respect to the principle of independent review of the protocol and conduct of human participant research, the study identified five (5) relevant benchmarks or stipulations, namely: a mandate for ethics review for human participant research (prohibition of retroactive approvals), the presence of recognised ethics committees, clear provisions against conflicts of interest (CoI), potential prevention of "ethics shopping", and provisions for post-approval monitoring (*Table 8*). The provisions are contained in an array of local ethics and regulatory documents, including: the National Health Policy & Plan, the Research for Health Policy, the Clinical Trials Guidelines, the UL-PIRE Handbook, and the NREB Guidelines.

Table 8: *Protective/Ethical Stipulations in Local Documents*: *Independent Review*

Emanuel et al. Principle	**Protective/Ethical Benchmarks**	**Source (s)**	
		Document(s)	**Specific stipulation(s) & location(s)**
Independent Review	*Mandate ethics review for human participant research*; *prohibits retroactive approvals*	National Health Policy & Plan	**Section 4.15:** ethics committees to "apply approved guidelines and internationally accepted standards" in determining the "appropriateness" of health and social welfare research
		Research for Health Policy	**Section 2.5:** "research involving human participants needs to be reviewed by a capable Research Ethics Committee

			(REC)…"; MoH to "ensure" this (**section 5.1.1 (g))**
		Clinical Trials Guidelines	**Section 1:** Ethics is as important to the conduct of clinical trials in Liberia as the scientific consideration, especially when reviewing clinical trial protocols **Section 2.15:** ethical approval from an ethics committee should form part of a clinical trial application package **Section 4.12:** requires a detailed account of the ethical steps taken to guarantee the rights, safety, and welfare of participants of clinical trials in Liberia
		UL-PIRE Handbook	**Part IV, paragraph 1:** mandatory ethics review for all research involving human participants **Part IV subpart F (1st paragraph):** "retroactive concurrence" is strictly forbidden **Part VI subpart F:** final decision as to which study might require ethics approval or not, or indeed the type of approval needed, lies with the committee, and that where needed, clarifications should be sought from the committees
		NREB Guidelines	**Section 1.9:** final decision is also left with the ethics committee
	Presence of recognised ethics committees	Research for Health Policy	**Annex 3:** Government recognised ECs: the National Research Ethics Board of Liberia (NREB) and the University of Liberia – Pacific Institute of Research and Evaluation IRB (UL-PIRE IRB)
	Clear provisions against conflicts of interest (*CoI*)	Research for Health Policy	**Annex 2:** protocols being submitted "should clearly state who is sponsoring the research study and what interest they have in its outcome"
		Clinical Trials Guidelines	**Annex 2–4:** researchers and monitors to sign declarations, which amongst other things, states that they have no conflicts, as it relates to the protocol under consideration
		NREB Guidelines	**Section 2.2:** defines Conflict of Interest and states that "transparent processes to identify and manage actual and potential conflict of interest" should be established, and that any researcher with such conflicts "should immediately inform the NREB about the conflict" **Section 2.5:** requires a researcher to "disclose the amounts, sources or potential sources of funding in any research proposal and, following approval of the proposal, any subsequent funding sources"
		UL-PIRE Handbook	**Part VI subpart E (2):** conflicted members are expected to recuse themselves, except

			for the purpose of providing relevant information
	Potential prevention of "*ethics shopping*"	Research for Health Policy	**Section 5.1.3.1:** mandates NREB to "establish guidelines for the review of research for health protocols for use by other review boards"
	Provide for post-approval monitoring	Research for Health Policy	**Section 5.1.3.4:** ethics committees to "monitor the conduct of research for health to ensure compliance with approved protocol" **Annex 2:** plans for monitoring and supervision must be made clear
		Clinical Trials Guidelines	**Section 4.10:** demands total access to research facilities **Sections 8, 9, 10, 11:** stipulations relating to amendments, safety reporting (AEs, SAEs, and SUSARs), use of Data and Safety Monitoring setups, and quarterly reporting, respectively **Section 13:** may inspect these facilities to ensure that there is compliance with GCP and LMHRA requirements and to "take enforcement action where necessary"
		UL-PIRE Handbook	**Part VI subpart L (1–4):** that the IRB has the right to "audit any research project that has been previously approved..."
		NREB Guidelines	**Section 1.11**: description of reporting responsibilities; passive monitoring or self-report of researchers **Sections 2.10–2.11:** these post-approval monitoring scenarios are essentially in the form of amendments (section 2.10), and progress reports on the protocol, including reporting of safety parameters (section 2.11)

4.2.7 Principle 7: Informed Consent

Under the Emanuel et al. principle of obtaining informed consent, the study found three (3) relevant benchmarks, namely: a requirement for informed consent, a provision for consent/assent involving those with compromised or limited agency, and a provision for the use of unwritten/unconventional consenting means. As captured in *Table 9*, these provisions are contained in the cited sections of the following local ethics and regulatory documents: Constitution of Liberia?, Research for Health Policy, Clinical Trials Guidelines, Public Health Law, NREB Guidelines, UL-PIRE Handbook, Children's Law, and Child Welfare Policy.

Table 9: *Protective/Ethical Stipulations in Local Documents*: *Informed Consent*

Emanuel et al. Principle	Protective/Ethical Benchmarks	Source (s)	
		Document(s)	**Specific stipulation(s) & location(s)**
Informed Consent	*Requirement for informed consent*	Constitution of Liberia	**Article 11 (a):** "all persons are born equally free and independent"
		Research for Health Policy	**Section 2.5:** Defines informed consent; stating that it is a prime requirement when carrying out research with human subjects
		Clinical Trials Guidelines	**Section 6:** stresses the need for informed consent of participant or legally acceptable representative
		Public Health Law	**Sections 18.1, 18.21 (a), 18.21 (c)(iii), & 18.21 (e):** though mainly relating to therapeutic instances, these sections contain stipulations on voluntary informed consent
		NREB Guidelines	**Sections 2.3–2.4:** outline a guide to researchers when preparing a protocol for submission to NREB. The package, particularly for initial or "new submissions", must include a sample of the informed consent form to be used
		UL-PIRE Handbook	**Part VI subpart I:** "no human subject will be involved in research involving minimal or greater risk prior to obtaining informed consent in accordance with internationally acceptable standards"
	Consent/assent provision for those with compromised or limited agency	Children's Law	**Article 1 section 3:** defines child (>18 yrs) **Article 2 section 2.1:** "best interest of the child shall be the paramount consideration" **Article 2 section 2.2 (a)–(g):** catalogues a number of factors that should be given careful consideration, including any harm that has been suffered, the age, sex, background, physical, emotional needs etc **Article 2 section 3 (b):** a child is entitled to participate in this decision-making, "subject to his or her evolving capacities"
		Child Welfare Policy	**Section 2.4.3:** a child is entitled to participate in this decision-making concerning his/her best interest, "subject to his or her evolving capacities" **Section 6:** defines child (>18 yrs)
		Public Health Law	**Chapter 1.1 (g):** defines child (>18 yrs) **Section 18.21 ((c)(iii)) of Part II:** LARs can include parents, legal guardians, an adult offspring, spouse, or distant relatives
		UL-PIRE Handbook	**Part VI subpart B (7):** defines child (>18 yrs) **Part VIII subpart B:** definition of LAR and Assent; LAR can include parents, legal guardians, an adult offspring, spouse, or distant relatives

	Permit use of unwritten/unconventional consent	UL-PIRE Handbook	**Part IV subpart B:** in the case of exempted studies that pose no risk to participants, implied consent (verbally obtained or via a cover letter) may be acceptable

4.2.8 Principle 8: Respect for Recruited Participants and Study Communities

As it relates to the final Emanuel et al. principle of continuing respect for research participants and participant communities, the study found that the local documents contain about five (5) key stipulations, including: a clearly stated right to privacy and confidentiality, the presence of mandatory reporting requirements, an explicit right of refusal or withdrawal without penalty, a requirement for the provision of periodic updates, and a guarantee of treatment or insurance against research-related injury. The key documents containing these stipulations, as shown in *Table 10*, include: Constitution of Liberia, Penal Code, Research for Health Policy, Public Health Law, Clinical Trials Guidelines, Children's Law, NPHIL Act, LISGIS Act, NREB Guidelines, and UL-PIRE Handbook.

Table 10: *Protective/Ethical Stipulations in Local Documents*: *Respect for Recruited Participants and Study Communities*

Emanuel et al. Principle	**Protective/Ethical Benchmarks**	**Source (s)**	
		Document(s)	**Specific stipulation(s) & location(s)**
Respect for Recruited Participants and Study Communities	*Clearly stated right to privacy and confidentiality*	Constitution of Liberia	**Article 16:** no individual's "privacy of the person" shall be interfered with, except by order of a court
		Penal Code	**Part II Chapter 12 subchapter E:** unauthorised disclosure of "confidential information", constitutes first degree misdemeanour **Section 19.1:** outlaws the sinister use of various devices to surveil, photograph, record, amplify, and/or divulge information relating to a person, without their consent or without authorisation by law
		Research for Health Policy	**Annex 2:** researchers to state how they intend to "maintain confidentiality or anonymize patient data"
		Public Health Law	**Section 18.1 of part II:** defines "medical confidentiality" and stresses the need for such on the part of doctors, health agents, paramedical staff, health workers, laboratories, pharmacies or people of similar status
		Clinical Trials Guidelines	**Sections 6.11 (o) and 4.12.3:** call for respect for and protection of the confidentiality of research participants

		Children's Law	**Section 18.1:** guarantees the right to privacy for children
		NPHIL Act	**Part 6 section 6.2 (b), (c) and (d):** emphasis on respecting the privacy and confidentiality of citizens, when it comes to the performance of their functions
		LISGIS Act	**Sections 50A.8 (23) & 50A.21 (1)–(2):** emphasis on respecting the privacy and confidentiality of citizens, when it comes to the performance of their functions
		NREB Guidelines	**Sections 1.13 and 2.8:** address both the confidentiality expectation of board members, when performing their core functions, and for researchers relative to safeguarding the confidentiality of participants and the proper storage of study documents
		UL-PIRE Handbook	**Part V; Part VI subpart I (2 (e) and 6); Part VIII subpart C:** address both the confidentiality expectation of board members, when performing their core functions, and for researchers relative to safeguarding the confidentiality of participants and the proper storage of study documents
	Presence of mandatory reporting requirements	Children's Law	**Article 5 section 4.4:** "any service provider, parent and community or town member shall report sexual and other forms of abuse to the Police"
		Penal Code	**Section 16.9:** "a parent, caregiver, teacher, guardian nurse or service provider who, without reasonable excuse, fails to report a case of child abuse or neglect known to him or her is guilty of a second degree misdemeanor"
		Public Health Law	**Section 41.56 of Part 5:** a physician who treats someone that is or appears to be addicted to narcotic drugs has to fill up a form (Form A) and have said information reported to the Minister of Health within 48 hours
	Explicit right of refusal or withdrawal without penalty	Clinical Trials Guidelines	**Section 6.11 (m):** "participation in the trial is voluntary and that the participant may refuse to participate or withdraw from the trial, at any time, without penalty or loss of benefits to which the participant is otherwise entitled"
		UL-PIRE Handbook	**Part VI subpart I 2 (i):** "participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled"

	Require provision of periodic updates	UL-PIRE Handbook	**Part VIII subpart C:** informed consent should include statement that "significant new findings developed during the course of the research, which may relate to the subjects' willingness to continue their participation, will be provided to the subjects"
	Guarantee of treatment or insurance for research-related injury	Research for Health Policy	**Annex 2:** require treatment for research-related injury
		Clinical Trials Guidelines	**Sections 2.14 and 6.11 (j):** provision of a certified copy of insurance for injury resulting from research participation
		UL-PIRE Handbook	**Part VI subpart I (2 (g)):** an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of or where further information may be obtained

4.3 What are the Key Institutions Involved With the Review, Approval, and Monitoring of Health Research in Liberia?

The study also sought to find out the institutions that are pivotal to the governance of health research in Liberia, especially those that are serving to regulate, review, accept/approve, and monitor the conduct of health research. Mirroring the situation with the governance documents earlier, these institutions are sorted into two major categories, namely: 1) regulatory or legal (Research Unit of the Ministry of Health (RuMoH), the National Public Health Institute of Liberia (NPHIL), and the Liberia Medicines and Health Products Regulatory Authority (LMHRA)); and 2) ethics institutions (National Research Ethics Board of Liberia (NREB) and the University of Liberia – Pacific Institute of Research and Evaluation Institutional Review Board (UL-PIRE IRB)), as revealed in *Table 11*. Some pertinent background information of some of these institutions is also captured in *Table 12*.

Table 11: *Key Local Institutions and their Roles*

ROLES	REGULATORY			ETHICS	
	LMHRA	R_uMoH	NPHIL	UL-PIRE	NREB
OVERSIGHT	X*	X	X	X	X
REVIEW	X*	X		X	X
APPROVE	X*			X	X
MONITOR	X*			X	X

Key
LMHRA=Liberian Medicines and Health Products Regulatory Authority; R_uMoH=Research Unit of Ministry of Health; NPHIL=National Public Health Institute of Liberia; NREB=National Research Ethics Board

*Clinical trials only

As clearly shown by *Table 11*, though all of these five (5) institutions are involved with the oversight of health research in Liberia, currently it is mainly the LMHRA, the UL-PIRE IRB, and the NREB that are involved with the review, approval, and monitoring of health research being conducted in the country; the MoH sometimes conducts what is referred to as "administrative review".

Table 12: *Key Background Information of Approval Institutions*

Parameters		Ethics		Regulatory
		UL-PIRE IRB	NREB	LMHRA
Year of Establishment		2005	2014	2010
Members	Scientist	2	19	9
	Non-scientist	5	2	1
	Comm. Rep.	0	1	1
	Total #	7	22	11
Type of Review	Scientific	YES	YES	YES
	Ethics	YES	YES	YES*
Review Template?		NO	NO	NO
Website	Present?	YES	NO	YES
	Address	http://www.ul-pireafrica.org/the-irb-policy-handbook/	____	www.lmhra.org
Registered?	Local	NO	NO	____
	Entity	___	____	
	Int'l	YES	YES	
	Entity	OHRP	OHRP	
SOP	Present?	YES	YES	YES
	Year of Publication	2008	2014**	2014

*Perform ethics review, but only as part of their evaluation process; **Document actually originally published in 2011

4.4 What are the Key Perspectives and Experiences of Stakeholders about Health Research Governance in Liberia?

Another line of inquiry for the study was to gauge the perspectives of key stakeholders, especially with respect to their knowledge and experiences of, as well as their roles in, the existent frameworks. Eleven (11) key stakeholders (*Table 1*) were involved in the study. From the analysis of the transcripts of the in-depth interviews, two key thematic perspectives emerged: the unclear nature of the governance system, along with the perceived inadequacy of the Liberian institutional and documentary frameworks. These major themes are presented and elaborated on below. Other valuable pieces of information are reflected in a supplemental table (Appendix 13). For the sake of comparison, views from representatives of oversight entities were compared with those of the researchers.

4.4.1 Unclear Nature of the Research Governance System

4.4.1.1 Less than optimal knowledge of major documents and contents

There seemed to be a relative lack of awareness or familiarity with the governance system or documents, on the part some stakeholders, with an awareness average of 64% (Appendix 15). Interestingly, researchers had a higher awareness average (73%), compared to representatives from oversight institutions (52%).

Additionally, the responses of some stakeholders with respect to a few specific stipulations did not seem to match what was in these documents. For instance, as reflected in Appendix 13, stakeholders were asked if they were aware of the existence of stipulations on research misconduct or abuse and the presence of mandatory reporting requirements in Liberia. On the issue of research abuse, only three (3) of eleven (11) rightly said "Yes", while eight (8) were either "unsure" (3) or responded with an absolute "No" (5). When compared with the findings of the documentary analysis, as captured in *Table 7*, a number of local documents were found to contain pertinent stipulations, something that the eight (8) respondents were either unsure of or thought never existed. Similarly, stakeholders were quizzed on the issue of the existence of mandatory reporting (Appendix 13). Of the eleven (11) participants, only 9 addressed the question.. Of that total amount (9), seven (7) respondents were either absolutely sure (7) that there were none, whereas one (1) was unsure about the presence of such requirements. Only one (1) person saying that said requirement existed.

4.4.1.2 Lack of clarity as to who does what

There appeared to be a lack of clarity, as it relates to governance entities and their core functions, as this observation illustrated:

> "*I think there should be some clarity on who is responsible to govern health research in Liberia*; *because I think it's not well understood right now*. *I think, you know, the LMHRA has knowledge of some level of responsibility, the MoH has some responsibility, perhaps NPHIL will have some level of responsibility, I don't know*. *But at this time, I'm not really clear on who is [who]…*" (*Researcher #2, female, 2018*).

This observation was confirmed by representatives of oversight entities, as one of them remarked:

> "*No...you are right, the awareness has been low, from the onset*. *So, we didn't have the communication department, so we right now have the communication department*. *And now, we are trying to decentralize most of our activities*" (*Entity 3 Rep, male, 2018*).

4.4.2 Inadequacy of Local Frameworks

4.4.2.1 Documentary frameworks

There was an overwhelming feeling, on the part of respondents (nine (9) out of eleven (11) = 82%) that the existent documents do not adequately address the ethical conduct of health research in Liberia, as indicated in *Figure 5*. This view from one of the respondents was representative of the vast majority of respondents:

> "*No... I would say they are not well comprehensive, in terms of protecting marginalized, disenfranchised, and vulnerable populations*. *I think those documents are generally generic in scope*; *[they] talk about the protection of human subjects, but not as detailed*" (*Researcher #6, male, 2018*).

Interestingly, this view did not seem to matter whether the respondent was from an oversight entity or a researcher, as Appendix 13 illustrates. It is important to add, also, that the one respondent who thought that the documents were adequate (*Figure 5*) was from one of the oversight entities, and might have felt the need to be defensive. But even in this case, it was still conceded, by this respondent, that:

> "*In terms of technology, in terms of modernization in research, our guidelines are not at the full extent of that…*" (*Entity #5 Rep, male, 2018*).

This view that the current documents are virtually silent on modern themes of the human research sphere was also shared by researchers, as indicated in the following response:

> "*I am familiar with these concepts [emerging concepts of bio-banking, genetic studies, and data sharing], but they are lacking*; *they are not elaborated in these guidelines that I just mentioned*" (*Researcher #3, male, 2018*).

Sadly, the referenced inadequacy in the documents is not only about the absence of technological or modern themes, but also extends to that of some contextually relevant issues. For instance, on the question of whether there are detailed guidelines on context-specific ethical issues like post-trial access, community engagement, and ancillary care obligations, the view of nine (9) of the ten (10) participants that gave a direct response (Appendix 13) was an unequivocal "No", as encapsulated in this response:

> "*No! There's no guidelines... Again we rely on international guidelines and international best practices, and PI's are made, in those meetings, to provide assurances that are documented*" (*Entity #1 Rep, male, 2018*).

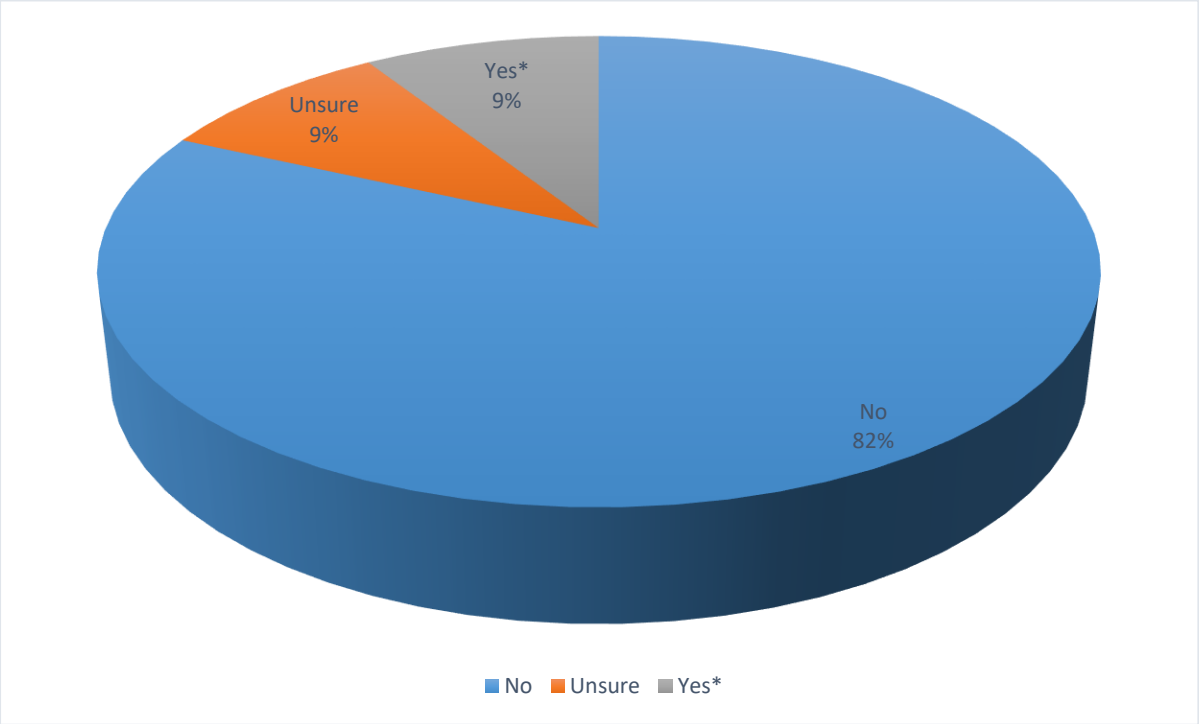

Figure 5: *Responses to adequacy of documents*

4.4.2.2 Procedural and institutional frameworks

4.4.2.2.1 Lack of active monitoring: "wild wild west"

In addition to the inadequacy of the documents, there were also concerns about the institutional and procedural inadequacies of the research governance framework. For instance, on the very significant question of the performance (oversight entities) or awareness (researchers) of active post-approval monitoring for approved protocols, only two (2) (18%) of the responses were in the affirmative; with the rest of the interviewees, nine (9) (82%) in total unequivocally responding 'No" (*Figure 6*). This view by one of the researchers was representative of the popular view:

> "*There's never been any; for all the research that I have conducted here, that I have submitted for ethical review, there's been naught. So, everyone is on their own, and it's one of the most dangerous environments you can think of. It's a terrible situation... It's like a wild wild west, if you want to put it like that*" (*Researcher #6, male, 2018*).

Even in the case of those who responded in the affirmative, there remained a sense that the exercise might not have been an actual monitoring visit, but more of a public relations exercise. This interviewee's lamentation underscored this point:

> "*I am not sure what they looked at. I just heard that there was an audit; so I didn't see an audit report, I don't know what they found, I don't know if they found any deficiencies*" (*Researcher #2, female, 2018*).

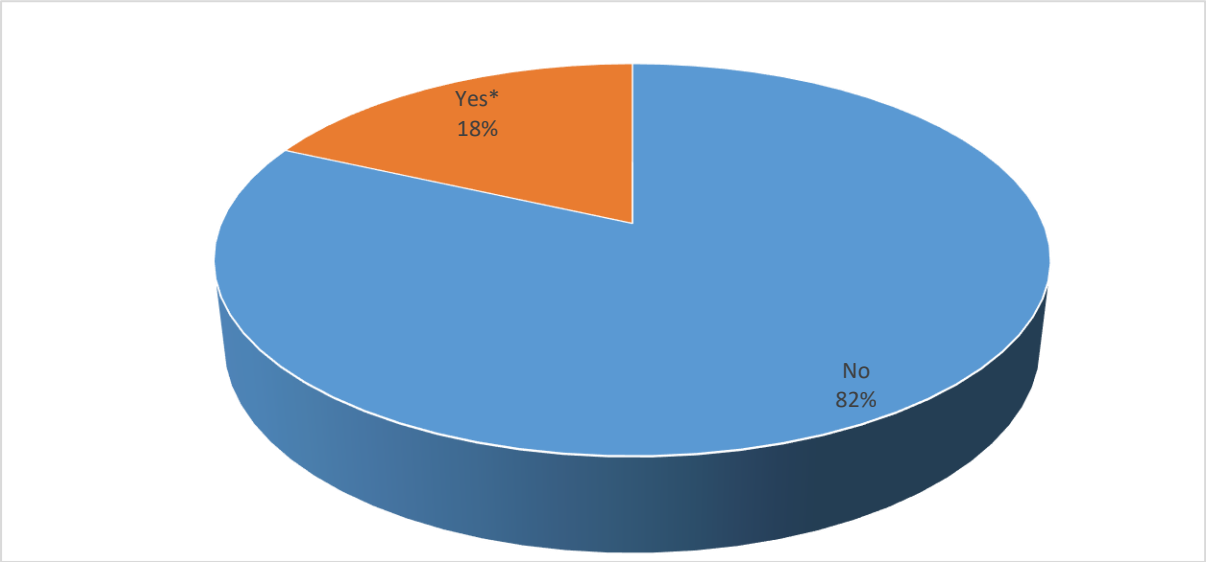

Figure 6: Performance/Awareness of Active Post Approval Monitoring

4.4.2.2.2 Lack of oversight entity

Another problem related to the institutional inadequacy domain concerns the lack of structural organisation of the research governance system. The somewhat fractured and seemingly uncoordinated layout of research governance, especially the absence of a central coordinating or overarching entity responsible for the hands-on governance of health research in the country, was highlighted, both from the interviews (Appendix 13) and from the review of the documents (Appendix 14).

4.4.2.2.3 Dissatisfaction with ethics committees

Furthermore, as pivotal as ethics committees are to the research governance system of the country, about four (4) of the five (5) researchers that responded (Appendix 13) were not satisfied with the ethics committees, as illustrated in this response

> "*No, I'm not satisfied. I'll tell you... 1*), *sometimes there's political interference*; *2*) *sometimes, the members of the ethics committee don't clearly understand the scientific validity or merits of some of these applications that are being reviewed, and sometimes, some members that are on the committee don't clearly understand the ethical implications of some of the things that are being reviewed within the context of the country*" (*Researcher #6, male, 2018*).

Even in the case of the one person who was supposedly "satisfied", this response leaves one feeling that there was a more sinister reason why:

> "*I mean yeah... From the point of view of the researcher, [giggling] I am satisfied*" (*Researcher #1, male, 2018*).

4.5 What Meaningful Recommendations Can Be Made to Improve the System, Moving Forward?

Finally, the study was also interested in finding out from stakeholders about what, in their experience, they thought was required to improve the research governance framework, moving forward. As clearly seen in *Figure 7*, the suggested actions mainly centered around 1) strengthening the documentary frameworks underpinning the governance of health research, and 2) improving the procedural or institutional support structures of research governance.

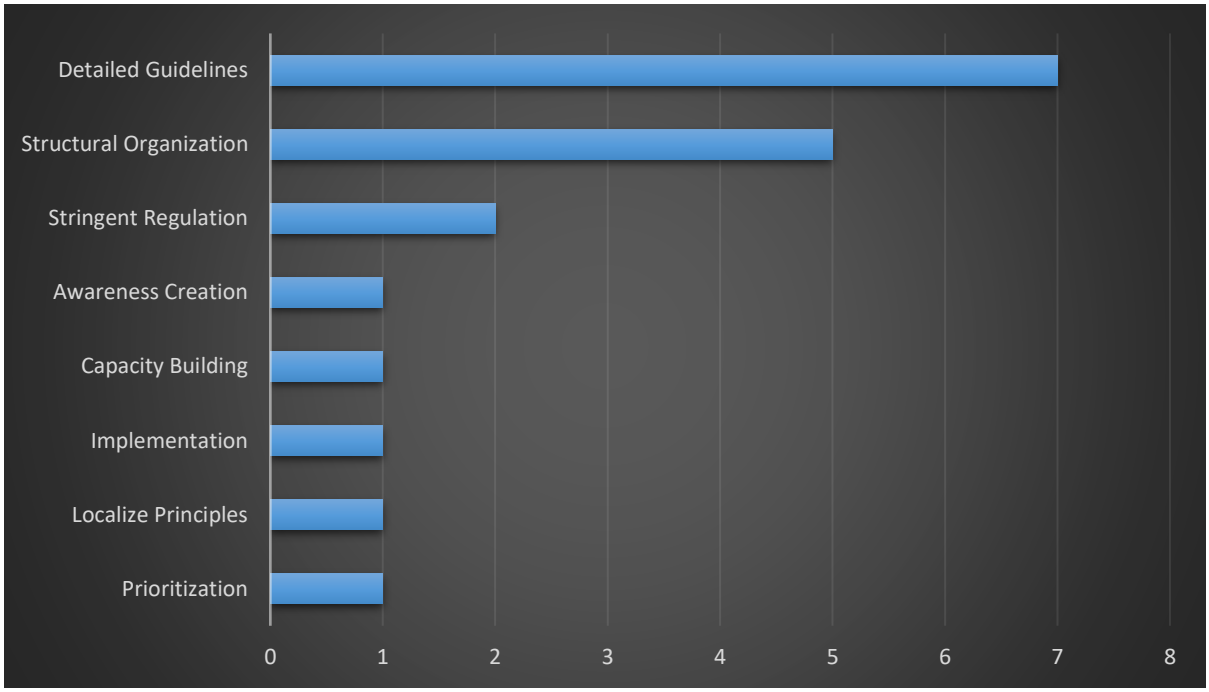

Figure 7: *Count of Needed Actions to Address Inadequacy*

4.5.1 Strengthening the Documentary Frameworks

Stakeholders suggested a range of steps to be taken address the referenced inadequacies. As presented in *Figure 7*, two (2) of the top three (3) most widely-referenced actions needed related to addressing the inadequacies surrounding the documents identified, i.e. addressing, in a stringent and detailed manner, areas of human participant research that are not addressed currently (data sharing, bio-banking, genetic/genomic studies), as well as adding some depth to the scantily-referenced aspects or those contextually relevant aspects that are absent. On the need for addressing scantily-referenced or absent issues, this view captured the feeling of the respondents:

> "*Look, if it's written and it's there, people do it! If you just say oh yes, we expect you to do it, if the guy doesn't do it, what do you do? You can't hold him, because it is not written anywhere and it's not a crime*" (*Entity #2 Rep, male, 2018*).

As it relates to the emerging issues, another respondent remarked:

> "*I think... the trend that I see research going now in Liberia, and in the sub-region, there is a critical need to now develop SOPs around our bio-repositories... sharing of human samples, whether alive or dead. Yeah... there is a need for researchers, or for ethics committees to start to develop special guidelines and procedures for the conduct of genomic studies or anything that has to do with specimens... or bio-specimens*" (*Entity #1 Rep, male, 2018*).

4.5.2 Improving the Procedural or Institutional Support Structures

4.5.2.1 Need for overarching entity for research governance

The following excerpt from one of the respondents lays out the essence of an overarching structure to oversee health research:

> "*One thing that needs to be developed first, or a structure that needs to be established first*; *Liberia needs a National Research Committee*. *That committee should serve as the overarching structure for every research in Liberia*. *So that Committee, when it exists, is also able to investigate malpractices*. *For example, the IRB could favour a particular paper and give ethical clearance*. *Who holds the IRB accountable? We need an institution that should do that*" (*Entity #5 Rep, male, 2018*).

4.5.2.2 Improving the function of ethics committees

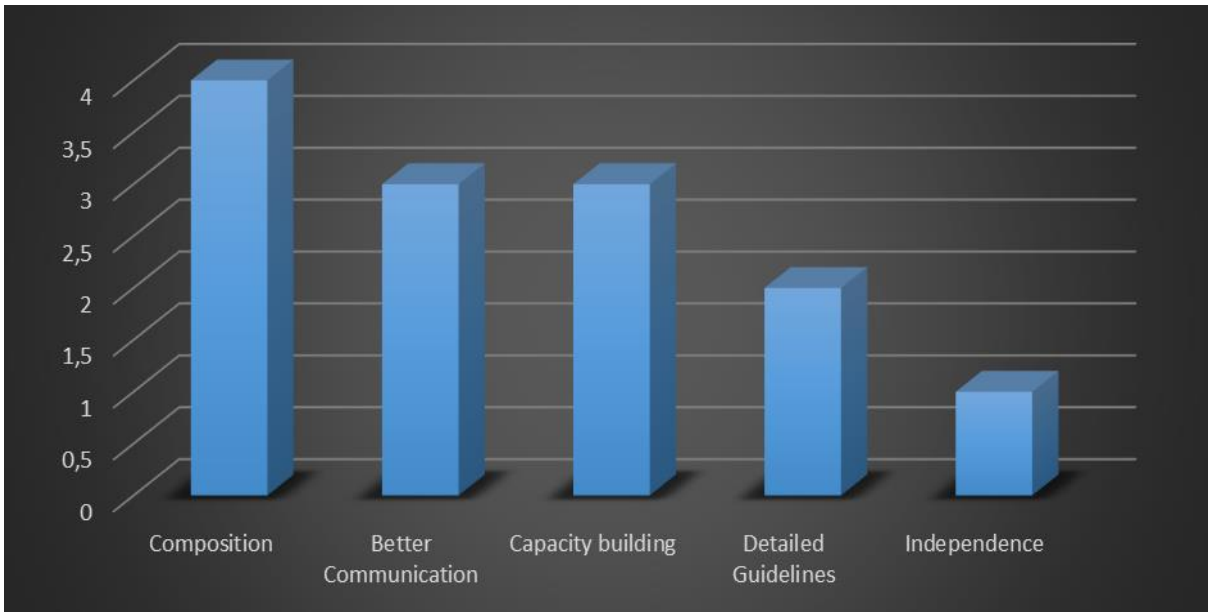

Figure 8: *Suggested Improvements for Ethics Committees*

As a means of rectifying some of the perceived and actual problems with the ethics committees, researchers suggested a range of actions that could help to improve the functions of these local committees, as reflected in Figure 8. The principal suggestions from respondents centered on improving their composition, enhancing better communication with researchers, and addressing the capacity problems that they face.

4.6 Summary

Using appropriate tables, graphs, and quotations, the results just presented have spelled out the list of institutions that are being used to govern the conduct of health research in Liberia, headed by the MoH, LMHRA, NPHIL, and two ethics committees. The chapter has also catalogued a number of protective stipulations which are contained or absent, as well as presenting the views and perspectives of stakeholders on the research governance frameworks being utilised in Liberia.

CHAPTER 5

DISCUSSION

This chapter deals with a discussion of results from this study, where the study's findings are fitted into current general literature or practice in similar contexts. It is laid out in three (3) sections. First, the institutional and documentary or policy frameworks underpinning the local governance of research, as found by this study, will be discussed. Next follows a discussion of the specific protective provisions that are locally guaranteed or absent, especially looking at them through the prism of the eight (8) Emanuel et al. (2004) principles and comparing them with specific stipulations of some of the major international guidelines (CIOMS, 2016; International Council for Harmonisation (ICH), 2016; Office for Human Research Protections (OHRP), 2010; The Nuremberg Code, 1948; World Medical Association (WMA), 2013). Lastly, the discussion will focus on the awareness level of the institutional and documentary or policy frameworks being used. At appropriate points, the perspectives of the stakeholders (contact persons and researchers) will be inserted, in order to give context to the written provisions in the local documentary and policy frameworks.

5.1 Key Institutional and Documentary Governance Frameworks

As laid out earlier, the provision of local oversight and governance of health research is cardinal, if research emanating from a country is to be considered ethical and acceptable (Andanda et al., 2011; Howell & Obado-Joel, 2016). This ensures that researchers and research institutions are not left to to their own devices to do as they deem appropriate, something that would represent a perilous option (Amdur, 2011; Huijstee & Schipper, 2011; Nwabueze, 2016), given the sordid history of research with humans. In this regard, ensuring that countries, especially those from low- and middle-income settings (like Liberia) have structural and documentary frameworks in place to oversee the ethical implementation of health research, cannot be overemphasised. The institutional and documentary frameworks governing health research in Liberia are discussed below.

5.1.1 Institutional Frameworks

The findings from this study highlight that five (5) institutions oversee, review, accept/approve, and monitor the conduct of health research in Liberia (Table 11). These institutions include three (3) linked with the Liberian Government (the Ministry of Health through its Research Unit (R_uMoH), the National Public Health Institute of Liberia (NPHIL), and the Liberia Medicines and Health Products Regulatory Authority (LMHRA)), and two (2) ethics institutions (National Research Ethics Board of Liberia

(NREB) and the University of Liberia – Pacific Institute of Research and Evaluation Institutional Review Board (UL-PIRE IRB)) that operate independently. Some pertinent background information of some of these institutions is also captured in *Table 12*.

By far the most important player when it comes to the governance of health research in Liberia, as in most other jurisdictions (Office for Human Research Protections (OHRP), 2018), is the Liberian Ministry of Health (MoH). According to section 39.3 of the Act creating the Liberian Ministry of Health (Ministry of Foreign Affairs, 2016), the Ministry is in charge of the "formulation, implementation, monitoring, and evaluation of health policies, plans and standard." More specifically, section 39.4 (c) of the Act empowers the Ministry to "coordinate and promote the conducting of health and health-related research". In order to ably discharge this mandate, the until-then dormant Research Unit (R_uMoH) was "re-established" in 2011 to oversee the management, coordination, and regulation of health research (Ministry of Health, 2018). Headed by a Director, the R_uMoH is the link between the government and all researchers and research institutions working in the country. Specifically, some of the key functions of the R_uMoH (including its representatives at county level), according to section 5.1.1 of the new research for health policy (Ministry of Health, 2018), include oversight of the entire research governance structure and performance of administrative review and acceptance (*Table 11*). Their oversight also includes guiding researchers as to which other institutions or line ministries they need to approach to apply for gate-keeping permissions, and which ethics or regulatory institutions they need ethics and regulatory approvals from.

In carrying out some of its management and coordination (oversight) activities, the MoH is, at least in theory, supposed to work hand-in-hand with the National Public Health Institute of Liberia (NPHIL) (*Table 11*). Though set up mainly as a conductor of public health research, the Act creating the Institute, specifically Part 2 section 2.3 (e), charges the Institute to "collaborate with the Ministry [of Health] to expand, conduct, and coordinate public health and medical research to inform Liberian public health policies" (Ministry of Foreign Affairs, 2017). The Act further empowers the institute to "collaborate with the Ministry and other relevant sectorial agencies to enforce environmental and public health laws, policies, and regulations" (Part 2 section 2.4 (a)(x)); "subject to approval of the Minister [of Health], set up Institutional Review Boards on public health and medical research" (Part 2 section 2.4 (a)(xix)); and "coordinate activities relevant to national specimen bank" (Part 2 section 2.4 (a)(xx)). Concerning review, acceptance/approval, and monitoring of research, the Institute appears to play no direct role.

For the review, approval, and monitoring of clinical trials (*Tables 11 & 12*), and the registration or licensure of drugs and medical devices in Liberia (LMHRA, 2014), the Liberia Medicines and Health Products Regulatory Authority (LMHRA) was created through an Act of the national Legislature, on September 30, 2010 (Ministry of Foreign Affairs, 2010). The Authority is headed by a Managing Director, appointed by the President of the Republic. Part 4 section 1.1 of the LMHRA Act stipulates

that the Authority is autonomous, reports directly to the President of the Republic, and shall submit an annual report of its activities to the Legislature. When it comes to specific responsibilities, section 2.1 (a)–(u) of Part 4 of the Act delineates all the duties and functions of the Authority, including the mandate to: "regulate the conduct of clinical studies of medicines and health products (j); and receive and investigate complaints regarding alleged violations of the Act or any regulations promulgated by the Authority, and impose appropriate sanctions in accordance with regulations promulgated by the Authority under this Act, and consistent with the Administrative Procedure Act of the Republic of Liberia and with due process of law (n)" (Ministry of Foreign Affairs, 2010) (p. 4).

In the discharge of oversight and governance functions, the aforementioned, mainly governmental entities are supported by the two nationally recognised ethics committees, mentioned earlier (Tables 11 & 12). The National Research Ethics Board (NREB), which was hastily set up by the Ministry of Health in 2014, at the height of the raging 2014 Ebola crisis, was meant to bring together a core group of scientists, non-science specialists, and community members to review protocols that were being submitted during this time, and for future submissions. In doing this, the Ministry co-opted the membership of the erstwhile Liberia Institute of Biomedical Research (LIBR) Ethics Committee and added additional members from other institutions. According to the 2018 Research for Health Policy (Ministry of Health, 2018), it is meant to morph into a national body that will develop guidelines for the guidance of other ethics committees. The University of Liberia – Pacific Institute of Research and Evaluation Institutional Review Board (UL-PIRE IRB), which was set up in 2005 (Table 12), is an international collaborative partnership between the University of Liberia, the premier government-owned University and a US-based research institution, the Pacific Institute for Research and Evaluation (Kennedy et al., 2006). The services provided by the UL-PIRE IRB are "available to persons or institutions interested in research work regarding the protection of human subjects in medicine or the social sciences in Liberia" (UL-PIRE IRB, 2008). Between these ethics institutions, there is an unwritten understanding that, according to revelations by stakeholders, the NREB is specifically in charge of biomedical research.

This local institutional set up in Liberia is no different from what is obtaining in several other countries on the African continent, especially with regards to the centrality of the Ministry of Health and the presence of a drugs regulatory authority and ethics review entities. A similar situation exists in nations like Kenya, Botswana, Malawi, and South Africa (Office for Human Research Protections (OHRP), 2018). One central difference currently, however, is the lack of an overarching entity with hands-on oversight of the conduct of health research, from national level, as came across in the interviews (Appendix 13) and the review of documents (Appendix 14). Whereas countries like Malawi, South Africa, Nigeria, and Kenya, have overarching entities like scientific councils/committees or national research ethics committees (Office for Human Research Protections (OHRP), 2018), such a structure is absent in Liberia. Moving forward, there is a need to modify the local institutional set-up in order to

accommodate such an entity, a point that came across clearly from the interviews with local stakeholders. As is reportedly the case in Cameroon, Nigeria, Malawi and Rwanda (Andanda et al., 2011), such a body could "oversee, register, and regulate ethics committees." As suggested earlier, discussions are underway to transform NREB into such an entity, though it might be allowed to retain its review, approval, and monitoring responsibilities, as happens in Malawi and Rwanda (Andanda et al., 2011).

The mere presence of local governance or oversight entities tasked with these responsibilities, as delineated earlier, does not necessarily mean that they executing these roles, at least in terms of efficiency. As presented in *Table 12*, some of these local committees lack functioning websites and even standard templates for the review of protocols submitted for review. The absence of a standard review template, for instance, means that there is no guarantee that similar protocols will receive similar reviews, as the quality of review would definitely be a function of the reviewers' preparedness and experience. Consequently, it is not surprising that an important result from the study is that there is an undercurrent of dissatisfaction with the performance of some of their responsibilities.

Though sometimes dissatisfaction with research ethics committees, especially from researchers engaged in social science research (Guillemin, Gillam, Rosenthal, & Bolitho, 2012; Page & Nyeboer, 2017; Schrag, 2011), is not uncommon, and can, in some cases, be predicated on peevish frustrations, it is nevertheless important to give serious consideration to this feedback. Given the central role played by ethics committees in the governance set-up, especially in a relatively research-naïve setting like Liberia, there is an absolute need for them to be not only properly constituted and functional, but also for them to enjoy the confidence of stakeholders, researchers included. Otherwise, this might possibly lead to some researchers avoiding the scrutiny of the review process, something that, according to the MoH (Ministry of Health, 2018), has been happening locally.

Additionally, it is undoubtedly the case that the ability of some of these institutions, for instance the ethics committees, to perform their prescribed functions is influenced by a myriad of factors, like the composition, funding and logistics, and the capacity of its members, etc. Therefore, the underlying challenges faced by these institutions cannot be corrected without stakeholder involvement. As suggested by researchers from the study, a range of actions could help to improve the functioning of these local committees, as reflected in *Figure 8*. The principal suggestions from respondents centered on improving their composition by recruiting more qualified reviewers, enhancing better communication with researchers, and addressing the capacity problems that experience. With respect to the need for capacity building, for example, it is important for local systems, especially in this era of collaborative research (IJsselmuiden et al., 2012; Ndebele, Wassenaar et al., 2014). For some understandable reasons, as captured by Klitzman (2012), the role played by local ethics committees,

and by extension other local regulatory authorities, who have their pulse on locally relevant and contextually appropriate research issues, cannot be overemphasised.

5.1.2 Documentary and Policy Frameworks

In addition to the institutional structures that are in charge of regulating health research in Liberia, another critical factor are the documents (policies, guidelines, regulations, laws) that are being used by these oversight entities to hold researchers accountable. Without the presence of proper legal and ethical documentary or policy frameworks to guide researchers, it could be considered they have *carte blanche* (Andanda et al., 2011; Sombié et al., 2017). As found by this study, there are five (5) major governance documents that are being used to regulate health research in the Liberia (*Figures 3 & 4*). As with the institutions earlier, three (3) of these major documents, namely: the Public Health Law (PHL), the National Research for Health Policy (RHP), and the Clinical Trial Guidelines (CTG)), while two (2), namely: the National Research Ethics Board (NREB) Guidelines and the University of Liberia – Pacific Institute for Research and Evaluation (UL-PIRE) IRB Handbook) are guidance documents from those local ethics committees (LMHRA, 2014; Ministry of Health, 2018; National Research Ethics Board, 2014; "Public Health Law Title 33 Liberian Code of Laws Revised", 1976; UL-PIRE IRB, 2008).

The Public Health Law is the highest health-sector law of the land and it is administered by the Ministry of Health of Liberia, according to section 39.4 of the Ministry of Health Act of 2016 (Ministry of Foreign Affairs, 2016). Adopted in 1976, the current law is divided into seven (7) parts, with different chapters and subchapters, dealing with a wide array of topics on hygiene, sanitation, and pollution; communicable and notifiable diseases and conditions, including their prevention, control, and reporting; narcotic drugs; the governance and regulation of medical and allied health professionals; and a range of other issues of public health significance. As a part of the health sector, the issue of the governance of health research, especially research involving human participants, supposedly also falls under this law. Interestingly, however, in terms of research-specific issues – like informed consent, risk-benefit assessments, requirement of ethics review, insurance for research-related injuries, etc. – the current law barely addresses them. It mainly deals with therapeutic and sanitary stipulations. It is therefore not surprising that, as shown by *Figure 4*, it has the least protective stipulations of the five (5) major documents, as determined by the analysis. Though this presents a serious challenge, since it is the highest health law of the land, with a degree of interpretational latitude, there are some pertinent provisions of the current law that have some research implications, as laid out later.

Another important document pivotal to the regulation of health research in Liberia is that of the National Research for Health Policy of 2018 (Ministry of Health, 2018). Written by the MoH, with the assistance of other key stakeholders in the country, it is the government's first major attempt to bring some

research-specific guidance to the sphere of health research and address evident challenges faced in the coordination and management of health research in the country. As explicitly stated in section 1.2 of this document, it "intends to establish a platform for research in Liberia by emphasising a more coordinated approach characterised by governance and management. It also sets out the rules and principles of research practices and procedures in Liberia and will ensure the highest standards of research activities in the country" (Ministry of Health, 2018) (p. 11). As can be observed from *Figure 4*, and will be illustrated later, the policy contains the most research-specific stipulations, even if some of these are just fleeting references to the issues.

With particular reference to the conduct of clinical trials in Liberia, the LMHRA's Guidelines for Clinical Trials (LMHRA, 2014) is another important source of ethical and legal guidance. Developed in 2014, the document is in fulfilment of the Authority's mandate to promulgate regulations to streamline, amongst other functions, the conduct of clinical trials in Liberia (Part IV section 2.1 (j) & (n) of the LMHRA Act) (Ministry of Foreign Affairs, 2010). The provisions in this document provide the minimum set of standards required for approval to conduct clinical trials involving medicines and health products in Liberia (section 1.0). Section 1.1 of the guidelines, stating the relevance of the document, indicates that it is intended to "provide Liberia with clearly expressed standards of good clinical practice in clinical studies that are also applicable to local realities and contexts and to ascertain that clinical trials carried out on human participants are designed and conducted according to strict scientific and ethical principles within the basis of good clinical practice" (LMHRA, 2014) (p. 1). By adopting the standard principles of the ICH-GCP guidelines, this local document lays a solid ground, at least in theory, for the protection of participants of clinical trials in the country.

Together with the three (3) government-linked documents described above, the guidelines of the two ethics committees are also pivotal in guiding health research in the country. Firstly, the NREB Guidelines (National Research Ethics Board, 2014), which was reportedly published in 2014, seems to have been essentially appropriated from the guidelines used by the erstwhile Liberian Institute for Biomedical Research Ethics Committee, published in 2011. It is divided into two (2) principal sections: 1) Administrative Procedures; and 2) Guide for Researchers. The Administrative Procedures section covers issues like meetings, decision-making methods, review types, decision types, etc. The second section deals with guides for and responsibilities of researchers, including submission types, reporting requirements, conflict of interests, etc. Taking its 2011 "publication" year into consideration, which would be eight years ago, this document is in serious need of revision, something that is reportedly being done currently.

The second ethics document is the UL-PIRE IRB Handbook, which governs the activities of the UL-PIRE IRB (elaborated on earlier), and was published eleven (11) years ago (UL-PIRE IRB, 2008). Though the actual handbook is not segmented into sections or parts, for the purpose of convenience,

the contents of the handbook are divided into eight (8) different parts which include: Part I: Introduction; Part II: Policy; Part III: Procedure; Part IV: University of Liberia Application Guidelines; Part V: Policy Statement on Confidentiality; Part VI: Institutional Review Board (IRB) Policy on Research Activities Involving Human Subjects; Part VII: The IRB Process; and Part VIII: Appendix Materials. Some of these parts have sub-categories or paragraphs that provide detailed information and guidance on the conduct of health research in the University and nationally. Again, as with the NREB guidelines, the time that has elapsed since the publication of this document is a serious concern. Given the rapidity and scale at which human participant research is advancing, this is a complete lifetime. This document needs updating to reflect the many new and emerging areas of health research.

5.2 Local Documents and Protective Provisions

Another key issue considered by the current study centred on the contents of local documents, in terms of specific protective stipulations contained in or absent from them. Results from the five (5) major documents (*Figure 3*), along with the ten (10) other pertinent national laws and policies (*Table 2*) indicate varying levels of important protective stipulations in these documents, as shown in *Figure 4*. Twenty-nine (29) different benchmarks were identified and are displayed in *Tables 3 to 10*, along with individual stipulations (quotations or summaries) associated with them, and the exact locations of the stipulations in the cited documents. The seven (7) benchmarks not found in the local documents are seen in Appendix 14 (blotted red). All of these benchmarks are under the Emanuel et al. (2004) framework alluded to earlier.

5.2.1 Provisions Guaranteed in Local Documents

5.2.1.1 Principle 1: Collaborative partnership

The Emanuel et al. principle of collaborative research mainly holds that research efforts or partnerships between researchers or sponsors, especially from higher income countries and authorities or communities from resource-limited settings, like Liberia, must be conducted in a fair, balanced, and ethical manner (Emanuel et al., 2004). As noted by Parker and Kingori (2016), there has been an acceleration of these sorts of research undertakings, which can sometimes be marred by a degree of imbalance between the mostly northern funders and mostly southern recipients. Interestingly, given the expensive nature of the research enterprise (Roback, Dalal, & Carlsson, 2011; Viergever & Hendriks, 2016), these collaborative arrangements appear to be the most feasible option, especially for a poor country like Liberia.

Under this principle, the first of the four (4) key protective benchmarks found in local documents assessed was the "Promotion of fair collaborative research partnerships". The results of this study have revealed that the local government is aware of the unbalanced nature of these collaborative partnerships, and has a desire to promote a degree of fairness in these arrangements, as described in the cited sections of the Research for Health Policy (*Table 3*). Interestingly, however, aside from an aspirational desire to ensure fairness, local documents are short on detailed guidance as to how such collaborative partnerships should be designed or implemented. This is a problem, because in the absence of carefully-crafted policies to guide these interactions, researchers from richer northern countries often try to impose their agenda (Parker & Kingori, 2016). In this regard, the research fairness initiative (Marais, Toohey, Edwards, & IJsselmuiden, 2013) presents a great platform for Liberian policy makers. This initiative is an attempt to help developing countries and well-meaning collaborating northern partners to overcome this challenge and guarantee some balance when these partnership agreements are being drawn up and implemented.

Another important benchmark identified in the Liberian frameworks, as depicted in (*Table 3*), is the "need for community involvement and synergic interactions with local authorities" when it comes to the different phases of the research cycle. A review of the key stipulations contained in some of these local documents (Research for Health Policy, National Health Policy & Plan, LMHRA Act, National Health Communication Strategy, and Public Health Law), as detailed in *Table 3*, reveals a general desire for a degree of involvement, consultation, openness, and synergy, in terms of relations with the communities, including local and national authorities. The paramount significance of this requirement for community participation and consultation with local authorities is to know what is culturally or legally appropriate in the context of research in the country. Contact with the requisite community and national institutions or authorities will make these contextually-appropriate aspects abundantly clear. As suggested by Guideline Seven (7) of CIOMS (2016), this is important not only for ethical reasons, but also for operational feasibility. Engagement of host communities and ensuring their buy-in and participation can result in the successful completion of research endeavours.

Also under the collaborative partnership is the "requirement for capacity building". The Liberian documents have an expressed requirement for the building of local capacity, when it comes to the conduct of research. As can be seen in *Table 3*, two (2) of the local documents (Research for Health Policy and Clinical Trials Guidelines) were found to highlight the importance of building local capacity when it comes to different aspects of the research enterprise. This requirement is in keeping with the general principle of beneficence, especially as it relates to the sharing of the benefits of research with participant communities. According to Guideline Eight (8) of CIOMS (2016), these collaborative research partnership arrangements should seek to improve the capacity of institutions in LMICs, both in terms of infrastructure and human resource. As a research-naïve country on the continent of Africa, where the need for capacity development in research has been highlighted (IJsselmuiden, Marais,

Becerra-Posada, & Ghannem, 2012), this cardinal requirement from the Liberian framework cannot be overemphasised. Sadly, Liberian research institutions rely heavily on external actors to drive this, as the government does very little, if any anything, to beef up capacity in the area of research. As made clear in the Research for Health Policy, Government's own research unit at the Ministry of Health does not have its own budget line item dedicated for this (Ministry of Health, 2018).

The final benchmark under this principle, as found by the study is the "requirement to comply with local laws/regulatory compliance". As contained in *Table 3*, the Research for Health Policy contains unequivocal calls for compliance with all of the local laws and guidelines, when conducting research in Liberia. Given the not-so-favourable history of research on human participants internationally, as elaborated on throughout this work, it is important that researchers conducting human participant research do so in accordance with what is legally permissible within each jurisdiction, a requirement that is supported by provisions in CIOMS and the Declaration of Helsinki (CIOMS, 2016; World Medical Association (WMA), 2013). As captured in the Declaration of Helsinki, research must be evaluated and overseen in accordance with "laws and regulations of the country or countries in which the research is to be performed as well as applicable international norms and standards" (p. 4).

5.2.1.2 Principle 2: Social validity

This principle, as described by Emanuel et al. (2004), calls for research done in low-resource settings to be targeted at solving social or health issues. Otherwise, it maintains that it would be unethical to put communities through the risk of a particular research endeavour that has no value to them. As presented in *Table 4*, there are three (3) key protective or ethical stipulations under the principle of social validity, namely: the need to prioritise and address local health needs, the requirement for results publication/dissemination and utilisation, and the need prevent the weakening of local systems.

As pointed out in the cited sections of the Research for Health Policy (*Table 4*), there is a local "need to prioritize and address local health needs". The government of Liberia has prioritised, at least on paper, research endeavours that are relevant to addressing the health needs of its citizens, and has admonished relevant stakeholders to follow suit. This stance is essential when it comes to ensuring that research in Liberia has social value, as is ethically required (Beauchamp & Childress, 2013; CIOMS, 2016; World Medical Association (WMA), 2013). Guideline Two (2) of CIOMS emphatically asserts that "before instituting a plan to undertake research in a population or community in low-resource settings, the sponsor, researchers, and relevant public health authority must ensure that the research is responsive to the health needs or priorities of the communities or populations where the research will be conducted" (p. 3).

Despite this unambiguous provision in the policy, however, the same document laments that there remains a huge disconnect between health needs of the country and scientific inquiry targeted at them. Section 1.1 of the policy indicates that most of the scientific investigations carried out in the country are not centred on core health issues that are afflicting the population. As a country still reeling from the twin crises of war and the 2014 Ebola outbreak, Liberia has woeful health indicators (Bjegovic-Mikanovic, Broniatowski, Byepu, & Laaser, 2019), and as such, these paper-based provisions have to be followed by tangible actions. It is probably due to this critical disconnect that the MoH, working in partnership with other stakeholders, has sought to put together a research agenda, which groups five (5) key domains (Maternal reproductive and child health, Communicable disease research, Non communicable Disease + NTDs. Healthy Lifestyles, Health system research, Communicable disease research) (Annex 6 of RHP), to begin the process of admonishing researchers and research institutions to scientifically delve into these areas and answer some of the important national health questions.

Another important local benchmark, under the principle of social value, is the requirement for "results publication/dissemination and utilization". As presented in *Table 4*, provisions in three local documents (Clinical Trials Guidelines, Research for Health Policy, and the UL-PIRE Handbook) indicate that researchers are expected to not only consider the dissemination and utilisation aspects of their research, but also to ensure this. It is also pointed out that steps are being taken to facilitate the documentation and sharing of research findings, to encourage the uptake of these findings into national policies to improve the lives of citizens. These stipulations and active steps taken are in keeping with similar requirements in some of the major guidelines like CIOMS (Guideline 24) and the Declaration of Helsinki (paragraph 36) (CIOMS, 2016; World Medical Association (WMA), 2013), which clearly require sponsors and researchers, in the interest of public accountability and social value, to ensure that research findings, including negative outcomes, are published. This requirement is especially essential in a country like Liberia, where the aforementioned RHP laments that until quite recently, most researchers, "due to the lack of policy and guidelines", were not likely to share findings of their scientific investigations with the MoH. This has effectively meant that critical findings from these investigations have not been used to inform policy changes or modifications.

Lastly, under this principle, the need to "prevent weakening of local system" is also suggested in one of the local documents. In Annex 2 of MoH Research Policy (*Table 4*), researchers are required to clearly outline the "resource implications to the host organization and any other involved departments" of their research activities. Though the reasoning is not clearly articulated in the policy, the essence of having such a disclosure is to gauge what implications the proposed study would have on existing systems and/or plans, to prevent negative impacts. This provision is one that is in line with CIOMS's (Guideline 8) caution against allowing research conducted in low-resource settings to "destabilize" the local health care systems (CIOMS, 2016). A provision like this is especially important because, in a country like Liberia – already saddled with a crippling disease burden and an abysmal patient-health-

worker ratio – the possibility of research endeavours taking resources away from the general health delivery system can have devastating consequences.

5.2.1.3 Principle 3: Scientific validity

The principle of scientific validity requires that a study conducted in low-income settings is appropriately designed and executed by academically and ethically qualified investigators, to ensure that the study would provide findings that are scientifically valid and have social value (Emanuel et al., 2004). Under this principle, the current study, as exhibited in *Table 5*, found three (3) key protective benchmarks. The first of these benchmarks is the "requirement for qualified and experienced investigators", as found in four (4) local documents (Public Health Law, Clinical Trials Guidelines, NREB Guidelines, and the UL-PIRE Handbook). Essentially, different sections of these documents require the registration and licensure of all allied health professionals (including those practising health research); require that researchers or study teams possess the relevant academic and ethical training, coupled with relevant professional experience; and in the case of multisite studies, a dedicated national investigator (*Table 5*). This benchmark and the provisions are consistent with standards that are set forth in some of the international guidelines (CIOMS, 2016; ICH Harmonised Guideline, 2016; The Nuremberg Code, 1948). These international guidelines maintain that it is ethically required that research involving human participants is designed and conducted by investigators who are qualified both ethically and scientifically. As unequivocally delineated in Guideline One (1) of CIOMS, "sponsors, researchers, and research ethics committees must ensure that all research personnel are qualified by virtue of their education and experience to perform competently and with integrity. This includes receiving appropriate ethics education and training" (p. 2). Because of the risks that could possibly be faced by participants in research, having investigators who are professionally and ethically qualified to identify and address possible harms is vital, especially given the history of research on humans.

In addition to addressing the need for research to be conducted by qualified investigators, another important benchmark, as found by the current study, is that some of the local documents (Research for Health Policy, Clinical Trials Guidelines, NREB Guidelines, and the UL-PIRE Handbook) collectively require a "clear and justified methodology". Specifically, these documents highlight the need for full explanation and justification of the methodological design and study procedures that will be utilised by any study being conducted in Liberia (*Table 5*). These provisions are also in keeping with stipulations in some international guidelines (CIOMS, 2016; International Council for Harmonisation (ICH), 2016; World Medical Association (WMA), 2013). A well thought-out design or methodology is not only important because it will determine the quality of data obtained and validity of the conclusions drawn, but also because of ethical considerations, as it would prevent subjecting research participants to

unwarranted procedures and prevent unnecessary expenditure. As noted by CIOMS (Guideline 1), "methodological shortcomings can derail promising avenues of research and squander valuable resources" (p. 2).

The final benchmark under this principle of scientific validity, as found by the current study, is the "requirement of prior knowledge". This benchmark, consisting of stipulations from three (3) of the national documents (Research for Health Policy, Clinical Trials Guidelines, and UL-PIRE Handbook), holds that research must be based on prior knowledge and address a genuine existing gap. Collectively, the documents, as presented in *Table 5*, allude to this necessity, and further require, in the case of clinical trials, that preclinical findings and data be presented. These provisions are in accordance with similar provisions found in The Nuremburg Code (count 3), Declaration of Helsinki (paragraph 21), and CIOMS (guideline 1) which require that scientific inquiries be based on prior knowledge or work done (CIOMS, 2016; The Nuremberg Code, 1948; World Medical Association (WMA), 2013). According to the Declaration of Helsinki, research has to "conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and adequate laboratory and, as appropriate, animal experimentation" (p. 4).

5.2.1.4 Principle 4: Fair selection of participants

As explained by Emanuel et al. (2004) this principle holds that the selection of participants for a study in LMICs should be based on fairness and the need to provide scientifically valid results that serve a social value. As presented in *Table 6*, there are three (3) key protective benchmarks under this principle, as found in local documents. The first of these benchmarks is the "requirement for fair and equitable selection", found in four (4) of the top five (5) documents (Research for Health Policy, Clinical Trials Guidelines, UL-PIRE Handbook, and NREB Guidelines). Essentially, these stipulations, as delineated in (*Table 6*), call for a justification for selecting a particular population, a clear description of the selection criteria, and absolute equity, when it comes to enrolment. These cited provisions are in tandem with the ethical principle of justice, which requires an equal distribution of the burdens and benefits of research participation (Beauchamp & Childress, 2013). Pursuant to this important principle, as noted earlier, research must aim for equal distribution of burdens and benefits of research; making sure to guard against the unequal or disproportionate selection of a group of people for research purposes, especially because of their vulnerability, either socially, economically, or cognitively, etc. It is a principle enshrined in some of the key international ethics documents like CIOMS (guideline 3), and ICH-GCP (6.5). CIOMS emphatically states that "groups, communities and individuals invited to participate in research must be selected for scientific reasons and not because they are easy to recruit because of their compromised social or economic position or their ease of manipulation" (p. 7).

The second important benchmark under this principle is a "clear definition for vulnerable persons", as laid out in *Table 6*. This is crucial because, to make a determination as to whether or not a study is observing the margins on the issue of "vulnerability", it is important to know who exactly qualifies as a vulnerable person, especially as set forth in the Liberian context. The most comprehensive definitions of vulnerable populations, including the case of "special vulnerability" for children, as suggested in *Table 6*, are contained in the appropriately-cited sections of Clinical Trials Guidelines, the UL-PIRE Handbook, and the Children's Law. These documents highlight, among other things, socio-economic, educational, hierarchical, and physical or mental factors in their definition of who constitutes vulnerable individuals, especially in the conduct of health research. The definitions contained in different Liberian guiding documents are consistent with those that are provided in several international guidelines like the Belmont Report, CIOMS, and ICH-GCP (CIOMS, 2016; International Council for Harmonisation (ICH), 2016; National Commission, 1979). As illustrated above and reflected in the following excerpt from CIOMS (p. 57), vulnerability in these international documents is mainly characterised by factors surrounding "impairments in decisional capacity, education, resources, strength, or other attributes" that are critical to a person's ability to further his/her own interests. To further stress the similarity between local and international guidelines on this issue, it is worth noting, in fact, that the definition used by the cited clinical trials guidelines of the LMHRA is an adoption of definition in the ICH-GCP Guidelines. In a country such as Liberia, which is notorious for having a poorly-educated, diseased, and impoverished population, a clear description of groups that are considered "vulnerable" is critical, if their interests are to be protected by the requisite institutions when conducting health research.

The third and final benchmark under the principle of fair selection of research participants, as found in local documents, is the unequivocal "requirement to ensure protection for vulnerable persons", as shown in *Table 6*, where provisions from the Research for Health Policy, Child Welfare Policy, Children's Law, and the UL-PIRE Handbook are highlighted. These cited provisions principally point to the need to avoid recruitment of vulnerable populations, and to ensure that special protections are provided, if they are recruited. In the case of children, their "best interest" is the paramount consideration, something that is the responsibility of everyone. Additionally, the establishment of a Child Welfare Committee and National Child Well-being Council, two groups that "exercise oversight on matters related to child well-being", has added a critical guarantee, at least in theory. For instance, when conducting research involving children, they could advise ethics committees on child-related welfare issues. These local protective provisions are in keeping with acceptable international best practice, when it comes to how and when to involve vulnerable individuals and groups in research, and the protections that must be provided (CIOMS, 2016; National Commission, 1979; World Medical Association (WMA), 2013). In accordance with provisions in the Belmont Report, involvement of vulnerable populations in research should be preceded by a careful assessment of the "appropriateness" of the study to the group, "including the nature and degree of risk, the condition of the particular

population involved, and the nature and level of the anticipated benefits" (p. 9). These international guidelines are also unequivocal about the need to actively protect vulnerable participants. As clearly espoused in the CIOMS guidelines, "when vulnerable individuals and groups are considered for recruitment in research, researchers and research ethics committees must ensure that specific protections are in place to safeguard the rights and welfare of these individuals and groups in the conduct of research" (p. 57).

5.2.1.5 Principle 5: Favourable risk-benefit ratio

The principle of favourable risk-benefit ratio is one of the important principles governing research with human participants. It is centred upon the principle of beneficence, along with the closely-related principle of non-maleficence (Beauchamp & Childress, 2013). Together these principles require that everything is done to mitigate the perceivable risks associated with a research endeavour, while at the same time maximising the benefits that could possibly be accrued from the research, be it for the individual participant, participant community, or humanity in general (Emanuel et al., 2004). Under this principle, this study categorised three (3) different ethical benchmarks or stipulations, as captured in *Table 7*.

The first of these three benchmarks is the explicit "requirement for favourable risk-benefit ratio". As apparent in *Table 7*, different ethics and regulatory documents in Liberia (Research for Health Policy, Clinical Trials Guidelines, NREB Guidelines, and the UL-PIRE Handbook) speak to the need to ensure a favourable risk-benefit ratio in health research, especially those involving human participants. The cited sections of the quoted documents (*Table 7*) stress the critical importance of having a favourable risk-benefit ratio from the start of the study to its conclusion, along with the need to clearly stipulate how this will be ensured, i.e. risk mitigated and benefits maximised. Provisions in these documents are in line with key sections of some of the referenced international documents like the Nuremburg Code, Declaration of Helsinki, ICH-GCP, Belmont Report, and CIOMS (CIOMS, 2016; International Council for Harmonisation (ICH), 2016; Office for Human Research Protections (OHRP), 2010; The Nuremberg Code, 1948; World Medical Association (WMA), 2013). As Guideline Four (4) of CIOMS clearly states, "before inviting potential participants to join a study, the researcher, sponsor and the research ethics committee must ensure that risks to participants are minimized and appropriately balanced in relation to the prospect of potential individual benefit and the social and scientific value of the research" (p. 9).

The second of these benchmarks relates to presence of "clear definition for risks and benefits". Table 7 reveals that two key local documents (Research for Health Policy and UL-PIRE Handbook) contain concise definitions of some of these concepts including, risk and minimal risk, benefits; along with a

delineation of different levels of risk (levels I, II and III). The significance of this is that in order to evaluate a risk-benefit ratio properly, there must, to some extent, be an understanding of what some of these key terms (risk and benefit) actually mean. The definitions for "risk" and "benefit" contained in the documents (*Table 7*) are consistent with the conventional definitions used in international human participant research (CIOMS, 2016; National Commission, 1979). For example, risk, according to Guideline Four (4) of CIOMS (2016), is said to be "an estimate of two factors: first, how likely it is that a participant will experience a physical, psychological, social or other harm; and second, the magnitude or significance of the harm" (p. 10). A similar case exists relative to the issue of benefits, with the Belmont Report referring to benefit as "something of positive value related to health or welfare" (p. 8). The presence of clear definitions for words enshrined in local documents, suggests that there is a uniform understanding of these concepts, and that people can be found wanting if their actions are deemed to have gone contrary to the wording and spirit of these definitions. They are not left to individual interpretations.

The final benchmark under this principle has to do with "provisions on handling research abuse or violations". A number of the documents reviewed (National Health Policy & Plan, Public Health Law, LMHRA Act, NREB Guidelines, and UL-PIRE Handbook) have very clearly laid out stipulations in this regard. As can be seen from the sections quoted in *Table 7*, these documents delineate the roles and responsibilities of different entities (MoH, LMHRA, Human Rights Commission, judicial authorities, professional boards, and ethics committees) as it relates to preventing, documenting, reporting, and addressing issues surrounding the rights and welfare of research participants (citizens). There are also suggested grievance resolution pathways, fines, and administrative actions, along with civil and criminal charges that could be brought to bear, given the type and magnitude of the violations suspected, or actually committed. As pointed out earlier, paragraph ten (10) of the Helsinki Declaration requires that researchers "must" conduct their research in accordance with local ethics and regulatory norms in their host countries (World Medical Association (WMA), 2013). This is especially important when it comes to ensuring the safety and welfare of research participants, and decisively handling any instances of violations or misconduct on the part of researchers. The presence, in the local documents, of these cardinal provisions against research abuse and violations is extremely important, especially as most of Liberia's citizens are poor and poorly educated, something that renders them vulnerable to exploitation. But even in situations where some issues are not adequately addressed locally, the Human Rights Act maintains that international agreements, to which Liberia is a party, can be invoked in appropriate circumstances. Similar human rights provisions have been reported in other African countries, like Uganda (Grant et al., 2005).

Though a number of these provisions relate to clinical practice, the overlap between clinical practice and research is oftentimes imperceptible. For example, a medical or allied health professional could also double as a researcher. An interesting feature of these provisions is the role of professional boards

in the handling of research misconduct or abuses, where they have oversight over their members. One challenge to this model is the fact that not all researchers might be members of professional boards. The question of what happens to non-medical researchers who are not members of any professional board remains unclear, a problem that has been identified in other African countries (Grant et al., 2005).

5.2.1.6 Principle 6: Independent review

This principle holds that for research to avoid or minimise conflict of interest situations and to enhance public accountability, it is important to have protocols go through independent and competent review from ethics committees and other regulatory institutions, depending on the nature of the research (Emanuel et al., 2004). With respect to this principle, the study identified five (5) relevant benchmarks or stipulations, as delineated in *Table 8*.

The first of these five (5) benchmarks is a clear "mandate for ethics review for human participant research and a prohibition of retroactive approvals", as contained in following local documents: the National Health Policy & Plan, Research for Health Policy, Clinical Trials Guidelines, UL-PIRE Handbook, and NREB Guidelines. These documents make it abundantly clear that, when it comes to the conduct of human participant research in Liberia, the application of internationally accepted ethical principles is essential; that review and approval of research protocols is a prerequisite to said research activity being conducted (no retroactive approval); and that the ethics committees retain the final decision regarding which studies require ethics review or not (*Table 8*). By providing for this important benchmark, the local documents are in line with international ethical norms and practices. As is now conventional, research involving human participants must be reviewed by a properly-constituted ethics committee, except where otherwise provided for (CIOMS, 2016; Office for Human Research Protections (OHRP), 2010; WHO, 2011; World Medical Association (WMA), 2013). In this regard, CIOMS's position leaves no doubt, stating: "all proposals to conduct health-related research involving humans must be submitted to a research ethics committee to determine whether they qualify for ethical review and to assess their ethical acceptability, unless they qualify for an exemption from ethical review (which may depend upon the nature of the research and upon applicable law or regulations). The researcher must obtain approval or clearance by such a committee before beginning the research" (p. 87). Without this requirement, researchers would literally have to rely on their own cognisance to determine the ethical acceptability of research, which, as made clear by earlier abuses, is no guarantee that the rights and welfare of research participants would be protected.

The second key benchmark relates to the "presence of recognized Ethics Committees" in the country. As listed in Annex 3 of the MoH's Research for Health Policy (*Table 8*) and discussed earlier (institutional frameworks), there are two active ethics committees currently recognised by the Liberian

government. They include the National Research Ethics Board of Liberia (NREB) and the University of Liberia – Pacific Institute of Research and Evaluation IRB (UL-PIRE IRB) (elaborated on earlier). This satisfies CIOMS's view that it is the "responsibility" of governments to "ensure" that "research is reviewed ethically and scientifically by competent and independent research ethics committees" (Guideline 8, p. 29). Though these are the only seemingly properly-constituted committees that are mandated to perform ethical and scientific evaluations of research protocols in the country, one or two hospitals reportedly have some arrangements for reviewing protocols that are to be implemented at their facilities, though as reflected in the Research for Health Policy just quoted, they are not fully recognised by the government. With respect to the two recognised committees, the extent to which they are truly capable of discharging these functions, *vis-à-vis* their compositions, competencies, and independence, is something that has to be independently ascertained. This is paramount, because the mere existence of a committee is no guarantee that its functions are in line with international best practice, or that it has all of the logistical and financial support to discharge its core functions (Soko, 2011). As a matter of fact, even though these ethics committees were not individually assessed, in terms of their functionalities (contained in their documents), the researchers interviewed, as part of the study, were not satisfied with the functioning of their committees (as discussed above).

The third benchmark under the principle of independent review pertains to "clear provisions against conflicts of interest (CoI)", as contained in the Research for Health Policy, Clinical Trials Guidelines, NREB Guidelines, and UL-PIRE Handbook (*Table 8*). Essentially, these documents contain a clear definition for CoI; require that researchers disclose and outline steps to address all potential and actual instances of conflicts of interest; and state that members of ethics review boards who might be in a conflicting situation, with respect to specific protocols, should recuse themselves. Though not clearly elucidated in these documents, especially in terms of its relevance to research, it is expected that disclosure of CoI situations, on the part of researchers or research institutions, would enable ethics boards to know whether researchers or institutions might be beholden to some external interest that could impact on the objectivity of the research process and compromise the integrity of the results drawn from the endeavour (CIOMS, 2016). It is necessary for ethics committees, according to Guideline 25 of CIOMS, to "develop and implement policies and procedures to identify, mitigate, eliminate, or otherwise manage such conflicts of interest" (p. 95). This is not only meant for researchers, as members of committees can also be highly conflicted, something that could seriously affect how they review research protocols.

The fourth of these benchmarks identified in the review, though indirectly, relates to the "potential prevention of 'ethics shopping', the phenomenon of researchers cherry-picking, based on convenience, which ethics committee reviews their study protocols" (Spellecy & May, 2012; Taylor, Ehrhardt, & Ervin, 2019). Though analysis revealed no direct mention of the issue, as quoted in *Table 8*, a provision of the Research for Health Policy (section 5.1.3.1), if followed through, could possibly prevent the

problem which, as one of the respondents in the stakeholder interview accepted, is something that some researchers engage in locally. Though this mandate is not elaborated upon, it is clear that the formulation of a uniform set of guidelines that will be used to guide the review of all local protocols would ensure, at least theoretically, that the quality of the review provided would not be reliant on which committee does the review, as all committees would be operating according to the same "guidelines". This local stipulation is in keeping with a stance advocated by CIOMS Guideline Eight (8), where it states that "regulatory or other governmental authorities must promote uniform standards for committees within a country" (CIOMS, 2016, p. 87).

The fifth and final benchmark under the principle of independent review relates to "provisions for post-approval monitoring". Whether passive or active, the issue of post-approval monitoring is heavily referenced in several local documents (Research for Health Policy, Clinical Trials Guidelines, UL-PIRE Handbook, and NREB Guidelines), as the stipulations presented in *Table 8* clearly illustrate. Together, these documents require researchers to clearly consider and lay out their plans for the continuous monitoring of their approved protocols, while also making clear provisions for local ethics and regulatory institutions to engage both in active (on site) monitoring and passive monitoring involving self-report of progress (continuing reviews), amendments, protocol deviations, and safety events (adverse events (AEs), serious adverse events (SAEs), suspected unexpected serious adverse reactions (SUSARs)).

These local stipulations are in conformity with the general international thinking on the issue of post-approval monitoring for human participant research. For instance paragraph 23 of the Helsinki Declaration and Guideline 23 of CIOMS are quite clear that research ethics committees must be authorised and allowed to monitor, mainly for safety and compliance purposes, previously approved studies (CIOMS, 2016; World Medical Association (WMA), 2013). As suggested by the preceding excerpt, the role of ethics committees and regulatory institutions in ensuring that research with humans is conducted in accordance with ethical principles does not end with review and approval of protocols. Following up on researchers, to ensure that the approved terms and conditions of a research protocol are being scrupulously adhered to, is also of paramount importance (CIOMS, 2016; International Council for Harmonisation (ICH), 2016; World Medical Association (WMA), 2013).

However, as aforementioned, the local frameworks seem to rely heavily on passive monitoring or self-reports, rather than on active or on-site monitoring. This is a problem that was corroborated by stakeholders during the interviews, where a vast majority of respondents, as reflected in *Figure 6*, indicated a lack of performance (in the case of oversight entities) or awareness (in the case of researchers). This lack of active post-approval monitoring in Liberia is similar to situations obtaining in countries like Zambia, Cameroon, among others (Andanda et al., 2011; Andanda et al., 2010; Nyika et al., 2009; Soko, 2011). Though the primary reasons (financial and logistical) for this situation are

understandable (Sombié et al., 2013), relying on passive monitoring, which is what mostly happens in Liberia (Appendix 13), is inadequate (Grant et al., 2005; Yao, Zhu, Jiang, & Xia, 2013), especially when it comes to clinical trials. Given the fragility and vulnerability of the country's impoverished citizens, the absence of active monitoring on the part of local oversight institutions, represents a serious concern for the welfare and safety of research participants. It is therefore encouraging that, as findings from this study show, there is 100% support for active monitoring (Appendix 13), a strong indication of where the country wants to go, resources permitting.

5.2.1.7 Principle 7: Informed consent

The principle of informed consent holds that the involvement of humans in research is predicated upon them being given all of the information pertaining to the study, in a language that they can understand, and, without any external pressure or influence, consenting to taking part in the study (Beauchamp & Childress, 2013). When working in low- and under-resourced settings, it is expedient, according to Emanuel et al. (2004), to take into consideration other factors like communities and their socio-cultural idiosyncrasies. With respect to the Emanuel et al. principle of obtaining informed consent, the study found three (3) relevant benchmarks, as captured in *Table 9*.

The first of the three (3) cardinal benchmarks under this principle is a clear "requirement for Informed consent". According to the findings of this study, all of the major ethics and regulatory documents (as found by this study – Research for Health Policy, Clinical Trials Guidelines, Public Health Law, NREB Guidelines, and the UL-PIRE Handbook), and the Constitution of Liberia, contain very pertinent stipulations for the requirement of informed consent or respect for individual bodily integrity and independence (autonomy), especially in the context of human participant research. As displayed in *Table 9*, the major documents contain a clear definition for informed consent, and make it unequivocally clear, that obtaining informed consent is a prerequisite for enrolling citizens of Liberia into research. These provisions are strongly supported by the constitutional guarantee that "all persons are born equally free and independent" (Article 11(a)). These local instruments demonstrate a clear recognition of the independence of individual Liberian citizens, and the need to have their voluntary and informed consent before enrolling them under any research protocol, similar to provisions in other African countries like Rwanda, Malawi and Zambia (Andanda et al., 2011). Voluntary informed consent is unarguably the foundational bedrock for research involving humans and, by guaranteeing this, local documents firmly comply with international best practice, as clearly provided for in almost all international ethics guidelines (CIOMS, 2016; National Commission, 1979; Office for Human Research Protections (OHRP), 2010; The Nuremberg Code, 1948; World Medical Association (WMA), 2013). As aptly pointed out in paragraph 25 of the Declaration of Helsinki, "although it may be appropriate to

consult family members or community leaders, no individual capable of giving informed consent may be enrolled in a research study unless he or she freely agrees" (p. 5).

Under the informed consent principle, the second significant local benchmark relates to "consent/assent provision for those with compromised or limited agency", something that is provided for in several local documents (Research for Health Policy, Clinical Trials Guidelines, Public Health Law, NREB Guidelines, and UL-PIRE Handbook), either by way of definition or direct guarantees (*Table 9*). These documents provide clear definitions for children, assent, and legally authorised representatives (LARs); require that assent, to the extent of their agency, is provided by those with limited or compromised agency; and that individuals consenting on their behalf should do so from the "best interest" perspective, especially in the case of children. These local stipulations concerning the role of legally authorised representatives and provision of assent (where applicable) in cases of limited or compromised agency, are essential in ensuring that the cardinal requirement of informed consent is maintained. They are also in accordance with provisions in some of the international guidance documents (CIOMS, 2016; Office for Human Research Protections (OHRP), 2010; World Medical Association (WMA), 2013). Guideline 16 of CIOMS, for instance, maintains that the relevant stakeholders of research must ensure not only that an appropriately-authorised individual provides consent, but also that the "assent of the subject has been obtained to the extent of that person's capacity, after having been provided with adequate information about the research at the level of the subject's capacity for understanding this information" (p. 61).

The final local benchmark under this principle relates to "permitted use of unwritten/unconventional consent", something that only the UL-PIRE Handbook (*Table 9*) elaborates on to any degree. According to the cited section of the Handbook, depending on the level of harm posed to research participants, verbal or implied consent may be acceptable. The IRB however maintains that an application package must first be sent to the IRB for prior approval of the use of the alternative consenting option or indeed the waiver of the documentation of informed consent process, as provided for in Guideline Nine (9) of the CIOMS guidelines (CIOMS, 2016). The significance of this provision is that other forms of consent, like community or verbal consent, apart from written or signed informed consent which is the conventional preference (CIOMS, 2016), depending on the situation, might be the most feasible. There is no mention of community consent in any of the documents, which is something that might need to be examined since, according to CIOMS, community consent or approval, in communal societies like Liberia, is expedient; though it must, in no way, serve as a substitute for individual consent.

5.2.1.8 Principle 8: Respect for recruited participants and study communities

This principle essentially maintains that the research study's obligations towards research participants do not come to an end after the participant has enrolled into a study; but that there must be continuous commitment to the participants or participant communities regarding their confidentiality/privacy, right to withdraw at any time, provision of medical care (ancillary or research-related), and post-trial obligations, like the sharing of findings or beneficial products of the study (Emanuel et al., 2004). As it relates to this final principle, the study found that local documents contain about five (5) key benchmarks, as shown in *Table 10*.

Under this principle, the first significant benchmark relates to the "clearly stated right to privacy and confidentiality", which is spelled out in a number of the legal and ethical documents (Constitution of Liberia, Penal Code, Research for Health Policy, Public Health Law, Clinical Trials Guidelines, Children's Law, NPHIL Act, LISGIS Act, NREB Guidelines, and UL-PIRE Handbook). As delineated in *Table 10*, these documents guarantee the right of individual citizens to confidentiality and privacy; outlaw the unauthorised recording and disclosure of personal information; and require researchers, ethics committees, and collectors of mass public data to put in place mechanisms to store and safeguard information collected in the discharge of their research or official responsibilities. These provisions clearly illustrate the position of local ethics and regulatory documents on the issue of privacy and confidentiality in the sphere of human participant research. They are undoubtedly in line with similar provisions in some of the principal international guidelines (CIOMS, 2016; International Council for Harmonisation (ICH), 2016; Office for Human Research Protections (OHRP), 2010; World Medical Association (WMA), 2013). As suggested in paragraph 24 of the Declaration of Helsinki and guaranteed in the Liberian frameworks, "every precaution must be taken to protect the privacy of research subjects and the confidentiality of their personal information" (p. 5). In countries like Liberia, where some socio-political or socio-cultural dynamics might expose an individual or a group to recriminations or stigmatisation, these provisions are essential, if research participants are to be shielded from the risk of facing negative consequences as a result of their participation in research or public information gathering exercises.

The second local benchmark of note under this principle is the "presence of mandatory reporting requirements", which, as explained in Guideline Twelve (12) of CIOMS (2016), is the case wherein "some jurisdictions require the reporting to appropriate agencies of certain communicable diseases or evidence of child abuse or neglect" (p. 51). It is one thing, in legal or regulatory terms, that impinges on the confidentiality requirement in research with humans. As presented in the quoted sections in *Table 10*, the analysis found that some local documents (Children's Law, Penal Code, Public Health Law) contain requirements for the reporting of instances of abuse, neglect, and addiction; in addition to spelling out that, in some cases, failure to report is a crime. Though some of these provisions might

mainly apply to therapeutic circumstances (as in the case of addiction), it could also have some research implications, especially if the person is being seen by a physician under research conditions. Substantively, though, the presence of these requirements has significant bearing on the conduct of research involving human participants. Knowledge of these mandatory requirements is important because they could have implications for confidentiality of information relating to research. A participant who is not keen to be referred to law enforcement authorities, for any reason, might understandably not be willing to participate in research that could possibly lead to criminal referrals. It is therefore expedient that information relative to such mandatory reporting requirements in Liberia is disclosed to research participants, as it might affect their willingness, or otherwise, to be enrolled in a particular protocol.

The third benchmark found by this study regards the "explicit right of refusal or withdrawal without penalty". As quoted in *Table 10*, the clearest language in this regard comes from the LMHRA's CTG and the UL-PIRE Handbook. These documents make it clear that participation by human subjects in research is under their control and that, in keeping with this, the decision to withdraw at any time is their choice, without those decisions incurring negative reprisals. This local provision is a fundamental aspect of the much-touted principle of respect for persons, and is clearly in agreement with almost identical provisions in international guiding documents like ICH-GCP, Declaration of Helsinki, 45 CFR 46, and CIOMS (CIOMS, 2016; International Council for Harmonisation (ICH), 2016; Office for Human Research Protections (OHRP), 2010; World Medical Association (WMA), 2013). Denying these rights to any potential or actual participant in a study is in direct contravention of the principle of autonomy, which as discussed by (Beauchamp & Childress, 2013), is the key tenant of the voluntary informed consent process that should continue throughout the study.

The fourth benchmark found in local documents concerns the "required provision of periodic updates", which deals with the issue of early significant findings that emerge during the conduct of a study. Contained in only one of the local documents (UL-PIRE Handbook) (*Table 10*), this provision, which is pursuant to the principles of continuing respect and beneficence, highlights the need for periodic assessment of the risk-benefit or risk-knowledge ratio, to ensure that if during the research process a significant finding is made/uncovered that could affect the continued enrolment of participants or indeed benefit them or their communities, researchers are obliged to share the information to the relevant parties for appropriate consideration. This also enables researchers to make real-time decisions as per the continuation of the study, as suggested in paragraph 18 of the Declaration of Helsinki (World Medical Association (WMA), 2013), where it is stipulated that "when there is conclusive proof of definitive outcomes, physicians must assess whether to continue, modify or immediately stop the study" (p. 3). However, as warned against in Guideline Four (4) of CIOMS, "decisions to stop a trial due to early, significant findings have to be balanced with the need to collect robust data on investigational interventions that are adequate to guide clinical practice" (p. 11).

The final benchmark under this principle centres on the stated "guarantee of treatment or insurance for research-related injury", which is contained in at least three (3) of the collected documents (Research for Health Policy, Clinical Trials Guidelines, and UL-PIRE Handbook), as captured in *Table 10*. These documents clearly require that researchers make provision for treating injuries that are suffered by participants, especially those related to the study, and that they are obliged to pass on information related to this treatment to potential and actual participants. These local guarantees are in keeping with principles of beneficence and non-maleficence, and their resultant requirement of providing coverage for the treatment of research participants who sustain injuries because of their involvement in the conduct of a research study (CIOMS, 2016; ICH Harmonised Guideline, 2016; Office for Human Research Protections (OHRP), 2010; World Medical Association (WMA), 2013). As clearly stated in Guideline Fourteen (14) of CIOMS, "sponsors and researchers must ensure that research participants who suffer physical, psychological or social harm as a result of participating in health-related research receive free treatment and rehabilitation for such harms, as well as compensation for lost wages, as appropriate" (p. 55). As further stressed by CIOMS, this should be guaranteed "regardless of fault," especially if the injury was sustained purely in furtherance of the aims of the research.

5.2.2 Protective Provisions Absent (Gaps)

As discussed above, the local ethical and regulatory documents contain several important traditional ethical issues that are considered and provided for. Issues like mandatory ethics review, informed consent, fair selection, favorable risk-benefit, and confidentiality are addressed, even if scantily at times. Despite this reality, there was an overwhelming feeling (nine (9) out of eleven (11) = 82%) among respondents that the documentary and policy framework governing health researching in the country, in terms of scope and depth, is inadequate, as depicted in *Figure 5*. Interestingly, this opinion *vis-à-vis* the inadequacy of the documentary framework was shared by respondents from both oversight entities and research institutions, as Appendix 13 illustrates. It is important to add, also, that even the respondent who thought that the documents were adequate, conceded that they were in need of "modernization". In terms of the specific areas of inadequacy, there were two specific concerns. First, in the local documents, there is a deafening silence on some of the key emerging issues confronting the conduct of research with human participants, especially in this modern age of research. Issues like genetic or genomic research, research with stored samples or bio-banks, data ownership, and data sharing, are evidently absent, an observation that was again confirmed by the respondents of the study.

The absence of these fast-emerging issues in Liberian documentary and policy frameworks is, unfortunately, shared by many other countries on the continent, as has been reported by a number of studies (Barchi & Little, 2016; de Vries et al., 2017; Klingstrom, Bongcam-Rudloff, & Reichel, 2017).

Given the many ethical challenges related to some of these issues, especially the limitations that they present with respect to the autonomy or informed consent principles (Emanuel et al., 2003), there exists an urgent need to incorporate some of these issues into local regulations and guidelines, which should be done in collaboration with communities and relevant stakeholders (Moodley & Singh, 2016; van Schalkwyk, de Vries, & Moodley, 2012). According to a recent Government of Liberia report, the Government has recently concluded plans to develop legislation on biosafety and biosecurity in 2019, to establish a bio-bank 2022, to train about 100 personnel on biosafety and biosecurity by 2022 (MoH/NPHIL, 2018). The taking of such local steps, *vis-à-vis* the fortification of local frameworks with respect to these emerging issues, is in conformity with the thinking of stakeholders interviewed in this study, as captured in the words of this respondent:

> "*I think... the trend that I see research going now in Liberia, and in the sub-region, there is a critical need to now develop SOPs around our bio-repositories... sharing of human samples, whether alive or dead. Yeah... there is a need for researchers or for ethics committees to start to develop special guidelines and procedures for the conduct of genomic studies or anything that has to do with specimens... or bio-specimen*" (*Entity #1 Rep, male, 2018*).

The second area of documentary inadequacy relates to the absence of some key contextually-relevant issues in local frameworks. As found from the review of key documents (Appendix 14; blotted red), there appears to be some noticeable gaps concerning issues like ancillary care, post-trial obligations, mechanism for resolving contentious findings, fair sharing of research benefits, and the use of local languages in the consenting process, amongst others. A similar impression was obtained from the respondents, majority (nine (9) out of ten (10)) of whom gave an unequivocal "No" when asked if detailed guidelines on these context-specific issues existed (Appendix 13). The following excerpt encapsulates the responses:

> "*No! There's no guidelines... Again we rely on international guidelines and international best practices, and PI's are made, in those meetings, to provide assurances that are documented*" (*Entity #1 Rep, male, 2018*).

This reference to international guidelines is a typical practice in Liberia, and in most cases would definitely suffice since many of these guidelines were designed with the true intention to protect research participants internationally. However, as pointed out earlier, the main drawback of relying on international guidelines is that they are mainly aspirational and lack enforceability, or indeed lack contextual considerations (Andanda et al., 2011; Nichols, 2016; Nuffield Council on Bioethics, 2002). This is something that needs to be addressed urgently. LMICs like Liberia have idiosyncratic realities that a one-oil-fits-all approach would not be advisable. In this regard, while suggesting a range of possible steps to address issues surrounding inadequacies identified within the documentary and policy

frameworks (*Figure 6*), stakeholders advocated for the development of stringent and detailed documentary frameworks in Liberia, something that accounted for two (2) of the top three (3) most widely referenced actions needed. As one respondent bluntly put it:

> "*Look, if it's written and it's there, people do it! If you just say oh yes, we expect you to do it, if the guy doesn't do it, what do you do? You can't hold him, because it is not written anywhere and it's not a crime*" (*Entity #2 Rep, male, 2018*).

5.3 Awareness Level of the Governance Frameworks

The mere existence of institutional and documentary frameworks is not sufficient; there must be awareness of the various components of these governance frameworks, i.e. the roles they play (institutions) or the specific stipulations that they contain (documents), especially when it comes to ensuring compliance. The results from this study are suggestive of a problem with the awareness level surrounding these frameworks, be it institutional or documentary.

With respect to governance institutions, especially those from the point of view of the Government, the study found a relative lack of clarity on the issue of which entities are responsible for doing what in the research governance system. Judging by some of the responses received, even experienced researchers still have a fundamental lack of clarity, as lucidly expressed by one of the respondents:

> "*I think there should be some clarity on who is responsible to govern health research in Liberia*; *because I think it's not well understood right now*. *I think, you know, the LMHRA has knowledge of some level of responsibility, the MoH has some responsibility, perhaps NPHIL will have some level of responsibility, I don't know*. *But at this time, I'm not really clear on who is [who]…*" (*Researcher #2, female, 2018*).

Though it can be argued that familiarising oneself with the different institutions, *vis-à-vis* what they do, is partly the responsibility of researchers operating within the country. One cannot overlook the fact that these institutions also have a cardinal role in educating researchers and research institutions, who are stakeholders and partners, as to who is responsible for what. Thankfully, this fact was not lost on some of the key oversight entities, as one representative remarked:

> "*No... you are right, the awareness has been low, from the onset*. *So, we didn't have the communication department, so we right now have the communication department*. *And now, we are trying to decentralize most of our activities*" (*Entity 3 Rep, male, 2018*).

When it comes to the documentary or policy framework, it became apparent, albeit it superficially, that there is a relative lack of awareness or familiarity with these important documents by some stakeholders. For instance, on the issue of familiarity with major local documents, the respondents' level of awareness, which was gauged by comparing their recollection of the local guiding documents with a pre-defined list of the major documents, reflects overall a far-from-optimal stakeholders' awareness average of 64% (Appendix 15), with researchers having a higher awareness average (73%) compared to representatives from oversight institutions (52%). Additionally, to gain some baseline insight into stakeholders' knowledge of the contents of existent guiding documents, their perspectives on few cardinal issues were compared with results from the content analysis of the documents. For instance, as reflected in Appendix 13, stakeholders were asked if they were aware of the existence of stipulations on research misconduct or abuse and of the presence of mandatory reporting requirements in Liberia. On the issue of research abuse, only three (3) of eleven (11) rightly said "Yes", while eight (8) were either "unsure" (3) or responded with an absolute "No" (5). When compared to the findings of the documentary analysis, as captured in *Table 7*, several local documents were found to contain pertinent stipulations, something that the eight (8) respondents were either unsure of or thought never existed. Similarly, on the issue of mandatory reporting, which was addressed by nine (9) of the eleven (11) respondents, eight (8) respondents were either absolutely sure that there were none (7) or unsure (1) about the presence of such requirements, with only one (1) person responding that said requirement did exist (Appendix 13).

Coupled with the general 64% awareness average of the major relevant local guiding documents (though the limited number of respondents adds a credible layer of doubt), the observed inconsistency between what the stakeholders "knew" and what was actually present in the documents represents a particular challenge, especially from a compliance perspective. The findings suggest a reason to believe that stakeholders' knowledge of some of the major documents and their contents might not be at a desirable level. This theme would be consistent with similar findings from Ogunrin et al. (2016). It is important to point out, however, that though some respondents did not name some of the key documents, this is by no means conclusive proof that they were totally unaware of them. It could have been due to oversight, or a misinterpretation of the question. Because of this possibility, a bigger study is needed to gauge how conversant most stakeholders are with local guiding documents, both type and content. But judging by these initial pointers, stakeholders have to endeavour to create more awareness (oversight entities), as suggested by the study respondents (*Figure 6*), while researchers must seek to familiarise themselves with the major institutions and documents as they relate to their cardinal functions and provisions. It is only by doing this that full compliance is ensured, or indeed areas needing modification can be identified and addressed.

On the observed difference between the researchers versus the representatives from oversight entities *vis-à-vis* awareness of the major documents, this could result from the fact that these researchers,

because they are the ones expected to comply with all of these documents, are under much more pressure to know all of them, as compared to the oversight institutions who are mainly concerned with the documents associated with their particular aspect of governance set-up. It also suggests that there might be limited interaction between research oversight institutions, a possibility that has been reported in other countries on the continent (Grant et al., 2005). This is an aspect that has to be corrected because, as suggested by Grant et al. (2005), this could mean that these oversight bodies might not "act collectively to protect and promote the rights of trial participants" (p. 19).

5.4 Summary

In this chapter, the results derived from the study were put into perspective, flowing from what is contained in the literature on the subject. Though there is semblance of a viable framework, both regulatory and ethical, there are key institutional and documentary gaps or inadequacies that require immediate attention. This feeling of inadequacy and the need for urgent action were issues that were loudly expressed by stakeholders, both from oversight institutions and conductors of research.

CHAPTER 6

CONCLUSION AND RECOMMENDATIONS

This chapter presents, in a systematic fashion, the conclusions of the study. Each distinct line of inquiry or research question is followed by the specific conclusion that the study draws as it relates to that question. It also presents, in a concise manner, the important contribution that this study has made to the body of knowledge. Additionally, the chapter lays out the shortcomings of the study, along with the recommendations for future studies, and a delineation of how the findings from this study can be made useful, when it comes to policy implications and important ways these results could be utilised.

6.1 Conclusion

This study set out to find out what ethical-legal documentary frameworks (guidelines, policies, procedures, regulations, and laws) govern health research in Liberia. Findings point to five (5) key documents, namely, the Research for Health Policy, the Public Health Law, the Clinical Trials Guidelines, along with Guidelines from the two (2) ethics committees (National Research Ethics Board (NREB) and the University of Liberia – Pacific Institute for Research and Evaluation IRB (UL-PIRE IRB)). In addition to these five (5) major instruments, few other documents also contain some very pertinent stipulations. The findings from this study represent the first time, at least nationally, that a concise list of local research governance documents has been assembled.

Another objective of the study was to audit, using a modified version of the Emanuel et al. framework, the selected documents in terms of the specific protections guaranteed in them, as it relates to the governance of health research in Liberia. From the systematic analysis of these major documents, it has been established that the guiding documents contain several of the core rudimentary ethics and legal requirements for the conduct of human participant research, including those of informed consent, mandated ethics review, favourable risk-benefit ratio, insurance for research-related injury, and penalties for research violations or abuse. These cardinal provisions notwithstanding, it has also been established that these documents are in need of depth and the inclusion of emerging aspects, like research with stored samples and bio-banking, genetic and genomic research, and data ownership and sharing, as well as addressing contextually-relevant issues, such as community participation, ancillary care, and post-trial access to approved interventions, mechanism for resolving contentious findings, fair sharing of research benefits, and the use of local languages in the consenting process, among others.

Additionally, the study also sought to get a clearer picture of which institutions or structures are involved in the review, approval, and monitoring of health research. In relation to this objective, the study found that five (5) key institutions, namely, the Ministry of Health (MoH), through its Research

Unit, the National Public Health Institute of Liberia (NPHIL), the Liberia Medicines and Health Products Regulatory Authority (LMHRA), the National Research Ethics Board (NREB), and the University of Liberia – Pacific Institute for Research and Evaluation Institutional Review Board (UL-PIRE IRB). The MoH and NPHIL mainly exercise management, coordination, and oversight functions, whereas the rest are centrally involved with the review, approval and, at least theoretically, post-approval monitoring of approved research.

Moreover, the study also set out to gauge the knowledge, perspectives, and experiences of key stakeholders – like the Ministry of Health, ethics and regulatory authorities, and current or former researchers – on the governance of health research in Liberia. In this regard, although there appeared to be some degree of obfuscation, there was a palpable feeling of inadequacy as it relates to the research governance system, both structurally and functionally.

Lastly, the study was also interested in soliciting, from the respondents, meaningful suggestions as it relates to improving the local health research governance system. With respect to this, stakeholders expressed an urgent need for the development of detailed and stringent guidelines, structural organisation to research governance, and the building of capacity for the conduct and governance of health research in the country.

6.2 Recommendations

Based on a careful review of assembled documents and the expressed views of study respondents, the following recommendations are hereby advanced, especially in an effort to proffer suggestions for policy and future research:

6.2.1 Recommendations for Policy and Practice

6.2.1.1 Need for adequate support for the research governance set up

There has to be a clear commitment from the Government and other interested parties to support the setting-up and strengthening (capacity building) of structures and processes to ensure ample protections for human participants of health research in the country. The mere existence of some of these structures is not sufficient; they must be made to work. This can only result from a deliberate decision to allocate funds for systems strengthening and capacity building.

6.2.1.2 Need for adoption of research fairness initiative

The problem with the power imbalance in north-south collaborative research undertakings is a very important one. This issue, while acknowledged in Liberia, has not been tackled with conviction. It is therefore expedient that national regulators and policy makers take deliberate steps to carve out the contours of this issue, as this phenomenon is bound to continue, especially in the post-Ebola research climate. An adoption of the research fairness initiative referenced above would be an effective first step.

6.2.1.3 Need for the establishment of an overarching entity

There is an urgent need for an entity to bring a semblance of order to the area of research governance. Such an overarching committee should be set up, preferably under the MoH, but should be largely autonomous to ensure independence. It should be tasked with drawing up policies and regulations to govern health research, addressing emerging areas like big data and data sharing, genetic and genomic research, research with stored biological samples etc., and should oversee the registration, licensing, and monitoring of ethics committees.

In this regard, it is being proposed that an overarching body for research, to be called the National Health Research Council (NHRC), be set up. To do this, one of two formulations could be utilised: 1) in the mould of the 1974 American Research Act (Amdur, 2011; Rice, 2008), the enactment of a stand-alone National Health Research Act, under which this council will be established, in addition to clearly delineating the different contours of conducting health research in Liberia, and enshrining stringent ethical and legal guard-rails; or 2) modify the current Public Health Law of Liberia, which is alarmingly silent on many key research-specific issues, to accommodate this council.

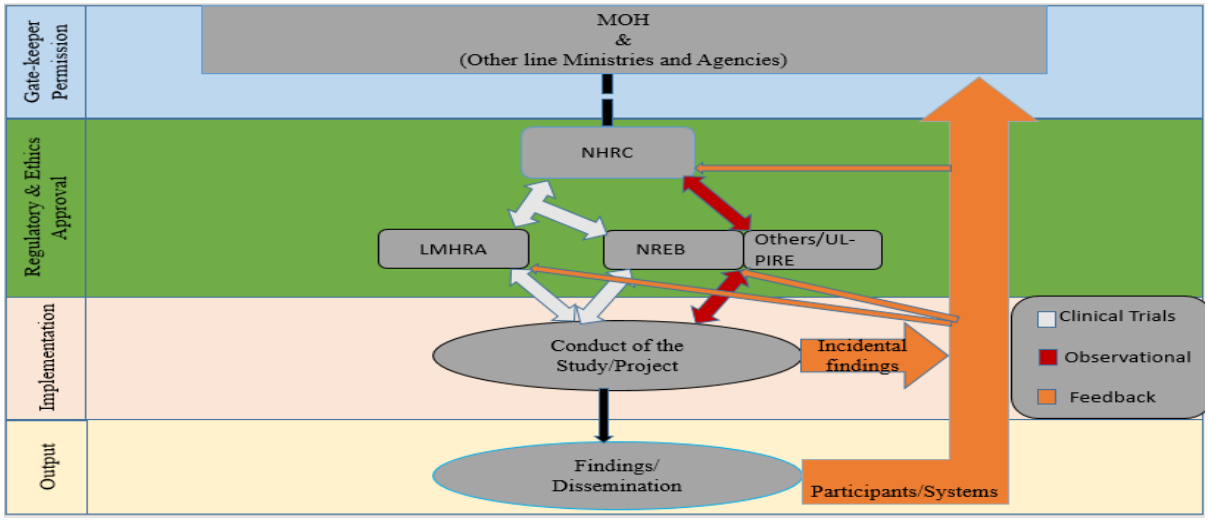

Figure 9: Proposed Research Governance Framework

6.2.1.4 Adaptation of a research governance structural framework

As found by this study, the governance system is in need of structural organisation. In a bid to address the problem of poor coordination and management of the research governance space, a four (4)-level research governance framework (diagrammed in *Figure 9* and described in Appendix 16) is being proposed. This framework conveniently separates the entire governance set-up into four clearly-defined general levels or stages, namely: 1) gate-keeper permission; 2) regulatory and ethical approval; 3) implementation; and finally, 4) dissemination or publication stage (output).

6.2.2 Recommendation for Future Research

One of the key aspects of this study was to establish which institutions are critical to the review, approval, and monitoring of health research in Liberia. While the study succeeded in doing so, the functionality of these institutions as it relates to their assigned responsibilities was not delved into. The existence, for example, of the ethics committees does not say much about the preparedness of these committees to perform, in an acceptable and effective manner, their core responsibilities. A future study to take a detailed look at these institutions and their preparedness to perform their core functions is recommended.

Another concern emerging from this study that needs additional investigative insight, is the degree to which stakeholders are conversant with the different ethics and regulatory documents, and the significant stipulations contained in them. There are some indications that stakeholders might not be sufficiently conversant. However, because this line of inquiry was not pursued by this study, there is a need some future research, especially with a larger pool of respondents.

6.3 Study Limitations

As with all studies, it is almost entirely impossible to execute a study without some limitations, especially as not all aspects of the study are ever under the direct control of the researcher. True to this, this study encountered a couple of limitations. Firstly, the number of interviews – eleven (11) key informant interviews, appears a bit inadequate. It is important to point out, however, that five (5) of those interviewed represented institutions, from which one contact person can reasonably provide the needed information. The other six (6) were active or former researchers who are conversant with the research landscape. As the inclusion of the researchers was mainly to obtain an indication of their experiences with the ethical and legal contours of health research in Liberia, the view was that six (6) would reasonably be enough to achieve that, after which responses may be redundant or repetitive.

Another challenge was the accessibility of documents. Given the fact that Liberia is still mainly operating on a paper-based level of documentation, there was difficulty accessing certain documents. To minimise the possible effects of this, a targeted online search, including the search of some major international databases was coupled with very diligent inquiries to the different concerned entities, all in an effort to obtain as many documents as possible. Despite all these efforts, it is possible that certain important documents might have been missed.

6.4 Conclusion

Designed principally to achieve the goal of clarifying the ethical and legal environment for the conduct of human participant research in post-Ebola Liberia, the current study has succeeded in bringing together a concise list of what is determined to be the key ethics and regulatory documents and institutions governing health research in the country. Additionally, the baseline audit of these key documents revealed that while containing most of the pre-requisite ethics and regulatory requirements for the successful conduct of health research, like the need for unfettered informed consent, the need to have research studies reviewed and approved by ethics committees, favourable risk-benefit ratio, insurance for research-related injury, and penalties for research violations or abuse, other pivotal issues, especially emerging issues like bio-banking, genomic studies, and data ownership are either not addressed or are addressed fleetingly. This somewhat incomplete or inadequate nature of the structural and functional components of the local research governance apparatus is something that was also stressed by the major stakeholders interviewed for this study.

Given the recent surge in the number of human participant research studies being conducted in Liberia, especially in the aftermath of the 2014 Ebola crisis, this study proposes some key structural and functional modifications to the local research governance system, along with the need for building local capacity. The baseline information provided by this study can go a long way in providing some useful clues as to what additional modifications need to be made to the research governance frameworks to ensure that the safety and welfare of present and future participants of health research are further enhanced. It is hoped that the Government and other interested stakeholders will help to institute policy changes, whereas civil society groups and rights advocates can use these findings to speak up for the observance of the rights and protections guaranteed in the local frameworks, while at the same time holding responsible parties accountable when they suspect system failures.

REFERENCES

African Health Observatory. (2014). Comprehensive Analytical Profile: Liberia. Retrieved from http://www.aho.afro.who.int/profiles_information/index.php/Liberia:Index Accessed: August 26, 2017.

Agnandji, S. T., Huttner, A., Zinser, M. E., Njuguna, P., Dahlke, C., Fernandes, J. F., . . . Siegrist, C.-A. (2016). Phase 1 Trials of rVSV Ebola Vaccine in Africa and Europe. *New England Journal of Medicine*, *374*(17), 1647–1660. doi: 10.1056/NEJMoa1502924

Ahmad, K. (2001). Drug company sued over research trial in Nigeria. *The Lancet*, *358*(9284), 815. https://doi.org/10.1016/S0140-6736(01)06011-1

Amdur, R. (2011). A brief history of IRB system. In R. Amdur & E. A. Bankert (Eds.), *Institutional Review Board Member Handbook* (3rd ed., pp. 7–18). Sudbury, Massachusetts: Jones and Bartlett Publishers.

Andanda, P. (2010). The role of law in the regulation of HIV-vaccine research in South Africa and Kenya. *African Journal of AIDS Research*, *9*(3), 249–259. https://doi.org/10.2989/16085906.2010.530178

Andanda, P., Awah, P., Ndebele, P., Onigbogi, O., Udatinya, D., & Mwondela, M. (2011). The ethical and legal regulation of HIV-vaccine research in Africa: Lessons from Cameroon, Malawi, Nigeria, Rwanda and Zambia. *African Journal of AIDS Research*, *10*(4), 451–463. https://doi.org/10.2989/16085906.2011.646660

Andanda, P., Gxoyiya, K., & Mahenge, O. (2010). The ethical-legal regulation of HIV vaccine research in Africa: A study of the regulation of health research in Cameroon, Malawi, Nigeria, Rwanda and Zambia to determine their capacity to protect and promote the rights of persons participating in HIV vaccine research. A report for the Ethics, Law and Human Rights (ELH) Working Group of the African AIDS Vaccine Programme (AAVP), commissioned by the World Health Organization (WHO).

Barchi, F., & Little, M. T. (2016). National ethics guidance in Sub-Saharan Africa on the collection and use of human biological specimens: a systematic review. *BMC Medical Ethics*, *17*(1), 64. https://doi.org/10.1186/s12910-016-0146-9

Beauchamp, T. L., & Childress, J. F. (2013). *Principles of Biomedical Ethics* (7th ed.). New York: Oxford University Press.

Beecher, H. K. (1970). *Research and the Individual Human Studies*.

Belotto, M. J. (2018). Data analysis methods for qualitative research: Managing the challenges of coding, interrater reliability, and thematic analysis. *The Qualitative Report*, *23*(11), 2622–2633.

BestPsychologyDegrees. (2018). The 30 most disturbing human experiments in history. Retrieved from https://www.bestpsychologydegrees.com/30-most-disturbing-human-experiments-in-history/ Accessed: August 31, 2018.

Bhat, S., & Hegde, T. (2006). Ethical international research on human subjects research in the absence of local institutional review boards. *Journal of Medical Ethics*, *32*(9), 535–536.

Bishop, C. (1995). Doctor in Zimbabwe race row out on bail. *BMJ* 1995;310:350. https://doi.org/10.1136/bmj.310.6976.350

Bjegovic-Mikanovic, V., Broniatowski, R., Byepu, S., & Laaser, U. (2019). Maternal and new-born health policy indicators for low-resourced countries: The example of Liberia. *South Eastern European Journal of Public Health* (*SEEJPH*). https://doi.org/10.4119/seejph-1890

Bowen, G. A. (2009). Document analysis as a qualitative research method. *Qualitative Research Journal*, *9*(2), 27–40.

Boyatzis, R. E. (1998). *Transforming qualitative information*: *Thematic analysis and code development*. Sage.

Braun, V., & Clarke, V. (2006). Using thematic analysis in psychology. *Qualitative Research in Psychology*, *3*(2), 77–101. doi: 10.1191/1478088706qp063oa

Carter, N., Bryant-Lukosius, D., DiCenso, A., Blythe, J., & Neville, A. J. (2014). The use of triangulation in qualitative research. *Oncology Nursing Forum*, *41*(5), 545–547. doi: 10.1188/14.onf.545-547

Centers for Disease Control and Prevention. (2009). Data collection methods for evaluation: Document review. Retrieved from https://www.cdc.gov/healthyyouth/evaluation/pdf/brief18.pdf Accessed: April 21, 2018.

CIOMS. (2016). International ethical guidelines for health-related research involving humans. Retrieved from http://dspace.ut.ee/bitstream/handle/10062/55438/web_cioms_ethicalguidelines2016.pdf Accessed: August 24, 2017.

Clark, E. G., & Danbolt, N. (1955). The Oslo study of the natural history of untreated syphilis: An epidemiologic investigation based on a restudy of the Boeck-Bruusgaard material a review and appraisal. *Journal of Chronic Diseases*, *2*(3), 311–344. https://doi.org/10.1016/0021-9681(55)90139-9

Clarke, V., & Braun, V. (2013). Teaching thematic analysis: Overcoming challenges and developing strategies for effective learning. *The Psychologist*, *26*(2), 120–123.

Das, N. K., & Sil, A. (2017). Evolution of ethics in clinical research and ethics committee. *Indian Journal of Dermatology*, *62*(4), 373–379. doi: 10.4103/ijd.IJD_271_17

de Vries, J., Munung, S. N., Matimba, A., McCurdy, S., Ouwe Missi Oukem-Boyer, O., Staunton, C., . . . Tindana, P. (2017). Regulation of genomic and biobanking research in Africa: a content analysis of ethics guidelines, policies and procedures from 22 African countries. *BMC Medical Ethics*, *18*(1), 8. https://doi.org/10.1186/s12910-016-0165-6

Emanuel, E. J., Wendler, D., Killen, J., & Grady, C. (2004). What makes clinical research in developing countries ethical? The benchmarks of ethical research. *The Journal of Infectious*

Emanuel et al (Ed.). (2003). *Ethical and regulatory aspects of clinical research*: *Readings and commentary*. Baltimore, Maryland, USA: The Johns Hopkins University Press.

Fischer, B. A. (2006). A summary of important documents in the field of research ethics. *Schizophrenia Bulletin*, *32*(1), 69–80. https://doi.org/10.1093/schbul/sbj005

Golafshani, N. (2003). Understanding reliability and validity in qualitative research. *The Qualitative Report*, *8*(4), 597–606.

Gomes, T. (2010). Nazi experiments. *Hohonu*, 13.

Grant, C., Lewis, M., & Strode, A. (2005). The ethical-legal regulation of HIV-vaccine research in Africa: A study of the regulation of health research in Botswana, Ethiopia, Kenya, Tanzania and Uganda to determine their capacity to protect and promote the rights of persons participating in HIV-vaccine research.

Guillemin, M., Gillam, L., Rosenthal, D., & Bolitho, A. (2012). Human research ethics committees: examining their roles and practices. *Journal of Empirical Research on Human Research Ethics*, *7*(3), 38–49. https://doi.org/10.1525/jer.2012.7.3.38

Hinman, A. R. (1998). Global progress in infectious disease control. *Vaccine*, *16*(11–12), 1116–1121. https://doi.org/10.1016/S0264-410X(98)80107-2

Howell, E., & Obado-Joel, J. (2016). Human subjects protection in the African context. *African Evaluation Journal*, *4*(1), a106. https://doi.org/10.4102/aej.v4i1.106

Huijstee, M., & Schipper, I. (2011). Organisations on the Radar: An exploratory study on outsourcing of clinical trials by pharmaceutical companies to contract research organisations in non-traditional trial regions Retrieved from https://papers.ssrn.com/sol3/papers.cfm?abstract_id=1759265 Accessed: January 3, 2018.

ICH Harmonised Guideline. (2016). Integrated addendum to ICH E6(R1): Guideline for good clinical practice E6(R2). Retrieved from https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R2__Step_4.pdf Accessed: September 25, 2017.

IJsselmuiden, C., Marais, D., Becerra-Posada, F., & Ghannem, H. (2012). Africa's neglected area of human resources for health research – the way forward. *South African Medical Journal*, *102*(4), 228–233. doi: 10.7196/SAMJ.5377

IJsselmuiden, C., Marais, D., Wassenaar, D., & Mokgatla-Moipolai, B. (2012). Mapping African ethical review committee activity onto capacity needs: The MARC initiative and HRWEB'S interactive database of RECS in Africa. *Developing World Bioethics*, *12*(2), 74–86. doi: 10.1111/j.1471-8847.2012.00325.x

International Council for Harmonisation (ICH). (2016). Integrated addendum to ICH E6(R1): Guideline for good clinical practice ICH E6(R2). Retrieved from https://www.fda.gov/downloads/Drugs/Guidances/UCM464506.pdf

Jenner, E. (1800). *An inquiry into the causes and effects of the variolae vaccinae, a disease discovered in some of the western counties of England, particularly Gloucestershire, and known by the name of the cow pox*: author.

Joffe, H. (2012). Thematic analysis. In D. Harper, & A. R Thompson (Eds.), *Qualitative Research Methods in Mental Health and Psychotherapy*: *A guide for students and practitioners* (pp. 210–223). Chichester: Wiley-Blackwell. https://doi.org/10.1002/9781119973249.ch15

Joffe, H., & Yardley, L. (2004). Content and thematic analysis. In D. F. Marks, & L. Yardley (Eds.), *Research Methods for Clinical and Health Psychology* (pp. 56–68). Sage Publications.

Jones, J. H. (2008). The Tuskegee syphilis experiment. In E. J. Emmanuel et al (Eds.), *The Oxford Textbook of Clinical Research Ethics* (pp.86–96). Oxford University Press.

Katz, J., Capron, A. M., & Glass, E. S. (1972). *Experimentation with human beings*: *The authority of the investigator, subject, professions, and state in the human experimentation process*. Russell Sage Foundation.

Kennedy, S., Harris, A., Oudemans, E., Young, L., Kollie, J., Nelson, E., . . . George-Williams, E. (2006). Developing capacity to protect human research subjects in a post-conflict, resource-constrained setting: procedures and prospects. *Journal of Medical Ethics*, *32*(10), 592–595. http://dx.doi.org/10.1136/jme.2005.014472

Kirigia, J. M., Ota, M. O., Motari, M., Bataringaya, J. E., & Mouhouelo, P. (2015). National health research systems in the WHO African Region: current status and the way forward. *Health Research Policy and Systems*, *13*(1), 1–14. doi: 10.1186/s12961-015-0054-3 (contains supplementary material, which is available to authorised users).

Kivunja, C., & Kuyini, A. B. (2017). Understanding and Applying Research Paradigms in Educational Contexts. *International Journal of Higher Education*, *6*(5), 26–41. https://doi.org/10.5430/ijhe.v6n5p26

Klingstrom, T., Bongcam-Rudloff, E., & Reichel, J. (2017). Legal & ethical compliance when sharing biospecimen. *Briefings in Functional Genomics*, *17*(1), 1–7. https://doi.org/10.1093/bfgp/elx008

Klitzman, R. L. (2012). US IRBs confronting research in the developing world. *Developing World Bioethics*, *12*(2), 63–73. https://doi.org/10.1111/j.1471-8847.2012.00324.x

Korstjens, I., & Moser, A. (2018). Series: Practical guidance to qualitative research. Part 4: Trustworthiness and publishing. *European Journal of General Practice*, *24*(1), 120–124. https://doi.org/10.1080/13814788.2017.1375092

Krans, B. (2013). Pain, Pain, Suffering, and the History of Human Experimentation. *Healthline News*. Retrieved from http://www.healthline.com/health-news/strange-the-sordid-history-of-human-experimentation-101213

Ledgerwood, J. E., DeZure, A. D., Stanley, D. A., Coates, E. E., Novik, L., Enama, M. E., . . . Graham, B. S. (2017). Chimpanzee Adenovirus Vector Ebola Vaccine. *New England Journal of Medicine*, *376*(10), 928–938. doi: 10.1056/NEJMoa1410863

Liberia Institute of Statistics and Geo-Information Services (LISGIS). (2009). 2008 National Population and Housing Census Final Results. Retrieved from http://www.emansion.gov.lr/doc/Population_by_County.pdf Accessed: September 20, 2017.

Liberia Institute of Statistics and Geo-Information Services (LISGIS). (2014). Liberia Demographic and Health Survey 2013. Retrieved from https://dhsprogram.com/pubs/pdf/FR291/FR291.pdf Accessed: September 20, 2017.

Lind, J., Stewart, C. P., & Guthrie, D. (1772). *A Treatise on the Scurvy*: Classics of Medicine Library.

LMHRA. (2014). Guideline for Application to Conduct of Clinical Trials in Liberia. Retrieved from https://clinregs.niaid.nih.gov/documents/liberia/G-LibClinTrial.pdf Accessed: August 27, 2017.

Macklin, R. (2005). Yet another guideline? The UNESCO draft declaration. *Developing World Bioethics*, *5*(3), 244–250. doi: 10.1111/j.1471-8847.2005.00122.x

Marais, D., Toohey, J., Edwards, D., & IJsselmuiden, C. (2013). *Where there is no lawyer*: *Guidance for fairer contract negotiation in collaborative research partnerships*. Geneva & Pietermaritzburg: Council in Health Research for Development (COHRED). Retrieved from http://www.cohred.org/wp-content/uploads/2012/04/Fair-Research-Contracting-Guidance-Booklet-e-version.pdf

Mbondji, P. E., Kebede, D., Zielinski, C., Kouvividila, W., Sanou, I., & Lusamba-Dikassa, P.-S. (2014). Overview of national health research systems in sub-Saharan Africa: results of a questionnaire-based survey. *Journal of the Royal Society of Medicine*, *107*(1_suppl), 46–54. https://doi.org/10.1177/0141076814530600

Ministry of Foreign Affairs. (2010). An Act to establish the Liberia Medicines and Health Products Regulatory Authority (LMHRA).

Ministry of Foreign Affairs. (2016). An Act to establish The Ministry of Health 2015. Monrovia.

Ministry of Foreign Affairs. (2017). An Act to establish The National Public Health Institue of Liberia.

Ministry of Health. (2018). *National Research for Health Policy and Strategy* (*2018–2023*).

MoH/NPHIL. (2018). *Joint National Action Plan for Health Security* (*NAPHS*) *2018–2022*. Retrieved from https://webcache.googleusercontent.com/search?q=cache:mwbm_DNKHBoJ:https://extranet.who.int/sph/republic-liberia-joint-national-action-plan-health-security-naphs+&cd=3&hl=en&ct=clnk&client=firefox-b-d

Moodley, K., & Singh, S. (2016). "It's all about trust": reflections of researchers on the complexity and controversy surrounding biobanking in South Africa. *BMC Medical Ethics*, *17*(1), 57. https://doi.org/10.1186/s12910-016-0140-2

National Commission. (1979). Belmont Report. *Office of Human Research Protections*. Retrieved from https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/index.html

National Malaria Control Program (2012). Liberia Malaria Indicator Survey 2011 Retrieved from https://dhsprogram.com/pubs/pdf/MIS12/MIS12.pdf Accessed: October 10, 2017.

National Research Ethics Board. (2014). Ethics Committee Guidelines: Procedures for Researchers. Retrieved from https://clinregs.niaid.nih.gov/documents/liberia/G-LIBR-NHSREC.pdf Accessed: August 26, 2017.

Nayyar, G. M. L., Attaran, A., Clark, J. P., Culzoni, M. J., Fernandez, F. M., Herrington, J. E., . . . Breman, J. G. (2015). Responding to the pandemic of falsified medicines. *American Journal of Tropical Medicine and Hygiene*, *92*(6 Suppl), 113–118. https://doi.org/10.4269/ajtmh.14-0393

Ndebele, P. (2013). The Declaration of Helsinki, 50 years later. *JAMA*, *310*(20), 2145–2146. doi: 10.1001/jama.2013.281316

Ndebele, P., Blanchard-Horan, C., Shahkolahi, A., & Sanne, I. (2014). Regulatory challenges associated with conducting multi-country clinical trials in resource-limited settings. *Journal of Acquired Immune Deficiency Syndromes* (*1999*), *65*(0 1), S29. https://doi.org/10.1097/QAI.0000000000000037

Ndebele, P., Mwaluko, G., Kruger, M., Ouwe Missi Oukem-Boyer, O., & Zimba, M. (2014). History of research ethics review in Africa. In M. Kruger, P. Ndebele, & L. Horn (Eds.), *Research Ethics in Africa*: *A Resource for Research Ethics Committees* (pp. 3–10) . Stellenbosch, South Africa: SUN Press.

Ndebele, P., Wassenaar, D., Benatar, S., Fleischer, T., Kruger, M., Adebamowo, C., . . . Meslin, E. M. (2014). Research ethics capacity building in Sub-Saharan Africa: A review of NIH Fogarty-Funded Programs 2000–2012. *Journal of Empirical Research on Human Research Ethics*, *9*(2), 24–40. https://doi.org/10.1525/jer.2014.9.2.24

Ndomondo-Sigonda, M., Miot, J., Naidoo, S., Dodoo, A., & Kaale, E. (2017). Medicines regulation in Africa: Current state and opportunities. *Pharmaceutical Medicine*, *31*(6), 383–397. https://doi.org/10.1007/s40290-017-0210-x

Nichols, A. S. (2016). Research Ethics Committees (RECs)/Institutional Review Boards (IRBs) and the globalization of clinical research: can ethical oversight of human subjects research be standardized. *Washington University Global Studies Law Review*, *15*, 351.

Nuffield Council on Bioethics. (2002). The ethics of research related to healthcare in developing countries. Retrieved from http://nuffieldbioethics.org/wp-content/uploads/2014/07/Ethics-of-research-related-to-healthcare-in-developing-countries-I.pdf Accessed: May 1, 2018.

Nwabueze, R. N. (2016). *Legal and ethical regulation of biomedical research in developing countries*. New York, USA: Routledge.

Nyika, A., Kilama, W., Chilengi, R., Tangwa, G., Tindana, P., Ndebele, P., & Ikingura, J. (2009). Composition, training needs and independence of ethics review committees across Africa: are the gate-keepers rising to the emerging challenges? *Journal of Medical Ethics*, *35*(3), 189–193. http://dx.doi.org/10.1136/jme.2008.025189

Office for Human Research Protections. (2010). Code of Federal Regulations: 45 CFR 46. Retrieved from https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html Retrieved: August 26, 2017.

Office for Human Research Protections. (2018). International Compilation of Human Research Standards. Retrieved from https://www.hhs.gov/ohrp/international/compilation-human-research-standards/index.html Accessed: September 21, 2018.

Office of the United Nations High Commissioner for Human Rights. (1976). International Covenant on Civil and Political Rights. Retrieved from https://www.ohchr.org/en/professionalinterest/pages/ccpr.aspx

Ogunrin, O. A., Daniel, F., & Ansa, V. (2016). Knowledge of the Nigerian Code of Health Research Ethics among biomedical researchers in Southern Nigeria. *Journal of Empirical Research on Human Research Ethics*, *11*(5), 397–407. https://doi.org/10.1177/1556264616650072

Okonta, P. I. (2014). Ethics of clinical trials in Nigeria. *Nigerian Medical Journal* : *Journal of the Nigeria Medical Association*, *55*(3), 188–194. doi: 10.4103/0300-1652.132035

O'Leary, Z. (2014). *The essential guide to doing your research project*: *Essential guide to doing research*. London, United Kingdom: Sage.

Page, S. A., & Nyeboer, J. (2017). Improving the process of research ethics review. *Research Integrity and Peer Review*, *2*, a14. https://doi.org/10.1186/s41073-017-0038-7

Parker, M., & Kingori, P. (2016). Good and bad research collaborations: Researchers' views on science and ethics in global health research. *PLOS ONE*, *11*(10), e0163579. https://doi.org/10.1371/journal.pone.0163579

Patton, M. Q. (1999). Enhancing the quality and credibility of qualitative analysis. *Health Services Research*, *34*(5 Pt 2), 1189–1208.

Polit, D., & Beck, C. (2012). Sampling in qualitative research. In D. Polit, & C. Beck (Eds.), *Nursing Research*: *Generating and assessing evidence for nursing practice* (pp. 515–528). Wolters Kluwer: Philadelphia.

Public Health Law Title 33 Liberian Code of Laws Revised, (1976).

Rice, T. W. (2008). The historical, ethical, and legal background of human-subjects research. *Respiratory Care*, *53*(10), 1325–1329.

Roback, K., Dalal, K., & Carlsson, P. (2011). Evaluation of health research: Measuring costs and socioeconomic effects. *International Journal of Preventive Medicine*, *2*(4), 203–215.

Sade, R. M. (2003). Publication of unethical research studies: the importance of informed consent. *The Annals of Thoracic Surgery*, *75*(2), 325–328.

Schrag, Z. M. (2011). The case against ethics review in the social sciences. *Research Ethics*, *7*(4), 120–131. https://doi.org/10.1177/174701611100700402

Soko, N. (2011). *Legal, policy and institutional frameworks regarding research ethics committees in Zambia* (Unpublished masters thesis). University of KwaZulu-Natal, Pietermaritzburg,

Sombié, I., Aidam, J., Konaté, B., Somé, T. D., & Kambou, S. S. (2013). The state of the research for health environment in the ministries of health of the Economic Community of the West African States (ECOWAS). *Health Research Policy and Systems*, *11*(1), 35. https://doi.org/10.1186/1478-4505-11-35

Sombié, I., Aidam, J., & Montorzi, G. (2017). Evaluation of regional project to strengthen national health research systems in four countries in West Africa: lessons learned. *Health Research Policy and Systems*, *15*(1), 46. https://doi.org/10.1186/s12961-017-0214-8

Spellecy, R., & May, T. (2012). More than cheating: Deception, IRB shopping, and the normative legitimacy of IRBs. *The Journal of Law, Medicine & Ethics*, *40*(4), 990–996. https://doi.org/10.1111/j.1748-720X.2012.00726.x

Spitz, V. (2005). *Doctors from hell*: *The horrific account of Nazi experiments on humans*: Sentient Publications.

Strode, A., Slack, C., & Essack, Z. (2010). Child consent in South African law: Implications for researchers, service providers and policy-makers. *South African Medical Journal*, *100*(4), 247–249. doi: 10.7196/SAMJ.3609

Strode, A., Slack, C., & Mushariwa, M. (2005). HIV vaccine research – South Africa's ethical-legal framework and its ability to promote the welfare of trial participants. *South African Medical Journal*, *95*(8), 598–601.

Tangwa, G. B., Browne, K., & Schroeder, D. (2018). Ebola vaccine trials. In D. Schroeder, J. Cook, F. Hirsch, S. Fenet, & V. Muthuswamy (Eds.), *Ethics Dumping*: *Case Studies from North-South Research Collaborations* (pp. 49–60). Cham: Springer International Publishing.

Taylor, H. A., Ehrhardt, S., & Ervin, A.-M. (2019). Public comments on the proposed common rule mandate for single-IRB review of multisite research. *Ethics & Human Research*, *41*(1), 15–21. doi:10.1002/eahr.500002

Tegli, J. K. (2018). Seeking retrospective approval for a study in resource-constrained Liberia. In D. Schroeder, J. Cook, F. Hirsch, S. Fenet, & V. Muthuswamy (Eds.), *Ethics Dumping*: *Case Studies from North-South Research Collaborations* (pp. 115–119). Cham: Springer International Publishing.

The Nuremberg Code. (1948). Retrieved from https://history.nih.gov/research/downloads/nuremberg.pdf

Tobin, G. A., & Begley, C. M. (2004). Methodological rigour within a qualitative framework. *Journal of Advanced Nursing*, *48*(4), 388–396. doi:10.1111/j.1365-2648.2004.03207.x

Triad 3. (2016). An introduction to document analysis. Retrieved from https://lled500.trubox.ca/2016/244 Acessed: April 20, 2018.

UL-PIRE IRB. (2008). POLICIES & PROCEDURES HANDBOOK Retrieved from http://www.ul-acre.org/wp-content/uploads/2013/03/UL-IRB-Policy-Handbook.pdf Accessed: August 26, 2017.

UNDP. (2018). Human development indices and indicators: 2018 Statistical update. Retrieved from http://hdr.undp.org/en/2018-update/download Accessed: June 1, 2019.

UNESCO. (2005). Universal Declaration on Bioethics and Human Rights. Retrieved from http://portal.unesco.org/en/ev.php-URL_ID=31058&URL_DO=DO_TOPIC&URL_SECTION=201.html; Accessed on July 10, 2018.

United Nations. (1949). Universal Declaration of Human Rights 1948. Retrieved from https://www.jus.uio.no/lm/un.universal.declaration.of.human.rights.../portrait.a4.pdf; Accessed: August 12, 2018.

United Nations. (1989). Convention on the Rights of the Child. Retrieved from http://www.ohchr.org/Documents/ProfessionalInterest/crc.pdf Accessed: September 16, 2017.

University of Missouri-Kansas City. (2017). History of research ethics. Retrieved from http://ors.umkc.edu/research-compliance-(iacuc-ibc-irb-rsc)/institutional-review-board-(irb)/history-of-research-ethics Accessed August 29, 2017.

van Schalkwyk, G., de Vries, J., & Moodley, K. (2012). "It's for a good cause, isn't it?" – Exploring views of South African TB research participants on sample storage and re-use. *BMC Medical Ethics*, *13*, 19. https://doi.org/10.1186/1472-6939-13-19

Viergever, R. F., & Hendriks, T. C. C. (2016). The 10 largest public and philanthropic funders of health research in the world: what they fund and how they distribute their funds. *Health Research Policy and Systems*, *14*(1), 12. https://doi.org/10.1186/s12961-015-0074-z

Walanj, A. S. (2014). Research ethics committees: Need for harmonization at the national level, the global and Indian perspective. *Perspectives in Clinical Research*, *5*(2), 66–70. doi:10.4103/2229-3485.128022

Washington, H. (2007). Why Africa fears western medicine. *New York Times*. Retrieved from https://www.researchgate.net/profile/Ha_Washington2/publication/259772857_08032007_06

59_AM_Why_Africa_Fears_Western_Medicine_-New_York_Times_r1orefslogin_Why_Africa_Fears_Western_Medicine/links/0c96052dceb1260842000000.pdf Accessed: August 28, 2017.

Weindling, P. (2001). The origins of informed consent: The international scientific commission on medical war crimes, and the Nuremberg Code. *Bulletin of the History of Medicine*, *75*(1), 37–71.

Weindling, P., von Villiez, A., Loewenau, A., & Farron, N. (2016). The victims of unethical human experiments and coerced research under National Socialism. *Endeavour*, *40*(1), 1–6. https://doi.org/10.1016/j.endeavour.2015.10.005

WHO. (2011). Standards and operational guidance for ethics review of health-related research with human participants. Retrieved from http://apps.who.int/iris/bitstream/10665/44783/1/9789241502948_eng.pdf?ua=1&ua=1 Accessed August 27, 2017.

Woodin, K. E. (2011). *The CRC's Guide to Coordinating Clinical Research* (2nd ed.). United States: CenterWatch.

World Medical Association. (2013). WMA Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects. Retrieved from https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/ Retrieved: August 26, 2017.

World Population Review. (2017). Liberia Population 2017. Retrieved from http://worldpopulationreview.com/countries/liberia-population/ Accessed: August 20, 2017.

Worldometer. (2017). Liberia Population (2017). Retrieved from http://www.worldometers.info/world-population/liberia-population/ Accessed: August 20, 2017.

Yao, B., Zhu, L., Jiang, Q., & Xia, H. (2013). Safety monitoring in clinical trials. *Pharmaceutics*, *5*(1), 94–106. https://doi.org/10.3390/pharmaceutics5010094

8.0 APPENDICES

8.1 Appendix 1: Information Sheet

Date:

Warmest greetings.

My name is Kokulo Franklin, a Candidate for a Master of Social Science degree in Health Research Ethics, from the University of KwaZulu-Natal in Pietermaritzburg, KwaZulu-Natal Province, Republic of South Africa.

You are being invited to consider participating, as an interviewee, in a study entitled "A Forensic Review and Evaluation of the Regulatory and Ethical Framework Governing Health-Related Research in Post-Ebola Liberia."

This study aims to determine the ethical-legal frameworks that are being used in the governance of health research in Liberia, assess the specific protections for research participants that are guaranteed therein, especially in the post-Ebola research context, and to proffer workable recommendations where needed. The study will mainly involve a baseline desk review of relevant documents. In addition to the review, there will also be ten (10) key stakeholder interviews, results from which will complement information derived from the desk review. The interview will be mainly centred on your knowledge and experiences of, and roles in, the existent frameworks.

Should you consent to participate, it is expected that the interview will last for at most two (2) hours. With your consent, the interview will be recorded and subsequently transcribed, to ensure that your responses are properly accounted for. This study is being sponsored by the South African Research Ethics Training Initiative (SARETI).

This study has been ethically reviewed and approved by the UKZN Biomedical research Ethics Committee (approval number_____) and the University of Liberia Pacific Institute for Research and Evaluation (UL-PIRE) (approval number _____).

At the conclusion of this study, results will be shared with relevant local authorities and other interested parties. Interested participants will also receive copies.

In the event of any problems or questions you may contact the researcher at 1st Floor, JFK Compound, 22nd Street, Sinkor, Monrovia, Liberia; email address: k_frank1980@yahoo.com/ franklinkok.80@gmail.com; cell phone numbers: +231886560914/+231777055965 or the UKZN Biomedical Research Ethics Committee, contact details as follows:

BIOMEDICAL RESEARCH ETHICS ADMINISTRATION
Research Office, Westville Campus
Govan Mbeki Building
Private Bag X 54001
Durban
4000
KwaZulu-Natal, SOUTH AFRICA
Tel: 27 31 2604769 - Fax: 27 31 2604609
Email: BREC@ukzn.ac.za

Or

Roland Bulu Martin,
Secretary
University of Liberia – Pacific Institute Research and Evaluation (UL-PIRE) IRB
UL-PIRE Africa Center,
Graduate School Building
University of Liberia
Capitol Hill, Monrovia
Liberia, West Africa
E-mail: martinbuludi@gmail.com

Participation in this study will be of no cost to you, apart from the time that you will take to participate in the interview. The study will provide no personal benefits to you for participation, apart from $ 10.00 USD worth of airtime, as a token of appreciation for your time. However, it is hoped that information derived from this study will contribute to the protection of the rights and welfare of actual and potential participants of health research, as it will try to find out what protections are guaranteed in the current ethical-legal frameworks and proffer workable suggestions for improvement of the system, where needed.

There is no anticipated harm that you could experience as a result of this study, apart from the issue of confidentiality. To guide against this potential problem, all interviews will be done at your convenience and at a time and place that fully guarantees the protection of your identity. No identifying information will be recorded. Recordings will be kept under lock and key, and shall be appropriately discarded after five (5) years.

Your participation in this study is completely voluntary, and at any time during the interview, you can choose to discontinue your participation with no consequence whatsoever.

Do you have any questions or concerns?

8.2 Appendix 2: Informed Consent

I, _____, have been informed about the study entitled "A Forensic Review and Evaluation of the Regulatory and Ethical Framework Governing Health-Related Research in Post-Ebola Liberia" by Mr. Kokulo Franklin of the University of KwaZulu-Natal in South Africa.

I understand the purpose of the study is to determine the ethical-legal frameworks that are being used in the governance of health research in Liberia, assess the specific protections for research participants that are guaranteed therein, and to proffer workable recommendations where needed; and that the study will mainly involve a baseline desk review of relevant documents, complemented by interview of some key stakeholders to gauge their knowledge and experiences of, and roles in, the existent frameworks.
I understand that the interview will last for at most 2 hours, and that the interview will be recorded, all pending my consent.

I have been given an opportunity to ask questions about the study and have had answers to my satisfaction.

I declare that my participation in this study is entirely voluntary and that I may withdraw at any time without any repercussions.

I have been informed that there are no personal benefits to be accrued from the study, apart from a token $ 10.00 USD worth of airtime, as appreciation for my time.

I know that if I have further questions/concerns or queries related to the study, I may contact the researcher at 1st Floor, JFK Compound, 22nd Street, Sinkor, Monrovia, Liberia; email address: k_frank1980@yahoo.com/ franklinkok.80@gmail.com; cell phone numbers: +231886560914/+231777055965.

If I have any questions or concerns about my rights as a study participant, or if I am concerned about an aspect of the study or the researcher, then I may contact:

BIOMEDICAL RESEARCH ETHICS ADMINISTRATION
Research Office, Westville Campus
Govan Mbeki Building
Private Bag X 54001
Durban
4000
KwaZulu-Natal, SOUTH AFRICA
Tel: 27 31 2604769 - Fax: 27 31 2604609
Email: BREC@ukzn.ac.za

Or

Roland Bulu Martin,
Secretary
University of Liberia – Pacific Institute Research and Evaluation (UL-PIRE) IRB
UL-PIRE Africa Center,
Graduate School Building
University of Liberia
Capitol Hill, Monrovia
Liberia, West Africa
E-mail: martinbuludi@gmail.com

I hereby voluntarily consent to participate in the above-mentioned study

_____ _____
Signature of Participant Date

Signature of Witness Date
(Where applicable)

Informed Consent: Audio Recording of Individual Interviews

In addition to agreeing to participate in the study, I give permission for audio recordings of the individual interviews to be used as data in this research project.

_____ _____
Name of Participant Date

_____ _____
Signature of Witness Date
(Where Applicable)

8.3 Appendix 3: Interview Schedule for Ministry of Health (MoH)

Thank you so much for agreeing to take part in this study, as a representative of the MoH. I am mainly interested in having a conversation with you on the governance of health research in Liberia, especially as it relates to getting the perspective of the Research Unit of the Ministry of Health, which is meant to streamline the conduct of health research in Liberia.

1) Which national documents (guidelines, policies, procedures, and laws) govern the conduct of health research in Liberia?
    a. Are these documents accessible?
    b. Do the documents require ethics review of all or some human participant research protocols?
        i. If yes for some human subjects research, describe which types
    c. Are these documents adequate?
        i. If no, what further regulations, in your experience, are needed to guarantee the ethical and legal conduct of health research?
2) Is there a pre-defined process (es) that must be followed by a researcher/research institution in order to conduct acceptable health research, particularly involving human participants?
    a. Can you outline said process?
3) Is the Research Unit/MoH playing any direct role, when it comes to the following aspects of regulating health research:
    a. Reviewing
        i. Scientific
        ii. Ethics
    b. Approving
    c. Monitoring
    d. If yes, what does this role involve:
        i. Reviewing
            1. Scientific
            2. Ethics
            3. Is said review independent of external institutional review?
        ii. Approving
        iii. Monitoring
    e. If no, do you think such functions are needed?
    f. If no, is there another agency or entity that is charged with said functions?
4) Is there a national entity that registers and monitors the activities of local ethics committees?
    a. If, no are there plans to establish one?
5) What is the stance of the Liberian ethical-legal frameworks on the below listed ethical issues:
    a. Insurance for research-related injury
    b. Post-trial access
    c. Ancillary care for research participants
    d. Community engagement/participation
    e. Standard of care
    f. Compensation for research participation
    g. Fair participant selection
        i. If they are not addressed by local regulations, how does the Ministry think such issues should be handled?

6) What legal safeguards are there against research misconduct/abuses?
    a. What needs to be done, if there are none?
7) In your experience, what is done when legal infractions (illicit drug use, child abuse, rape, etc.) are uncovered during research? Is there mandatory reporting?
    a. If not already required, do you think there should mandatory reporting?
8) What immediate plans does the ministry have, as it relates to regulating the ethical conduct of health research?
9) Is there anything else that you would like to bring to my attention?

THANK YOU FOR YOUR TIME AND PARTICIPATION

8.4 Appendix 4: Interview Schedule for Ethics Committee Administrators or Chairs

Thank you so much for allowing your entity to form a part in this study. I am mainly interested in getting some basic facts about your ethics committee, especially as it relates to its composition and review of protocols.

1) Entity Number _____
2) Year of establishment: ____
3) Composition:
    a. Number of members _____
    b. Scientists ____, Non-science specialists____, Community Members ____
4) Is your committee registered with any national or international body?
        a. Which national or international entity (ies)?
5) Which national documents (guidelines, policies, procedures, and laws) govern the conduct of health research in Liberia?
        a. Are these documents accessible?
        b. Do the documents require ethics review of all or some human participant research protocols?
            i. If yes for some human subjects research, describe which types
        c. In your view, are these documents adequate?
            i. If no, what further regulations, in your experience, are needed to guarantee the ethical and legal conduct of health research?
6) In your experience, what is done when legal infractions (illicit drug use, child abuse, rape, etc.) are uncovered during research? Is there mandatory reporting?
        a. If not already required:
            i. Do you think there should be mandatory reporting?
            ii. How do you usually handle such cases?
7) Does your committee perform both scientific and ethical review of protocols?
        a. If NO, what usually happens?
        b. To ensure consistency, does your committee have a standardized:
            i. List of requirements for protocol application?
                1. What are these requirements
                2. Are they easily accessible?
            ii. Framework for ethics review of protocols?
                1. What is the nature of such framework?
8) Is there any form of post-approval monitoring?
        a. If yes,
            i. What form does it take
            ii. What is the frequency of such monitoring?
        b. If no,
            i. Do you think such monitoring is needed?
            ii. What form should it take?
9) In your experience, what is the stance of the Liberian ethical-legal frameworks on the below listed ethical issues:

a. Insurance for research-related injury
b. Post-trial access
c. Ancillary care for research participants
d. Community engagement/participation
e. Standard of care
f. Compensation for research participation
g. Fair subject selection
    i. If they are not addressed by local regulations, how do you usually handle such issues?

10) In your experience, what legal safeguards are there against research misconduct/abuses?
    a. What needs to be done, if there are none?

11). Is there anything else that you would like to mention that we may not have covered?

THANK YOU FOR YOUR TIME AND PARTICIPATION

8.5 Appendix 5: Interview Schedule for LMHRA

Thank you so much for agreeing to take part in this study, as a representative of the LMHRA. I am mainly interested in having a conversation with you on the governance of health research in Liberia, especially as it relates to the role of LMHRA.

1) What is the role of LMHRA in the regulation of health research in Liberia?
    a. Which national documents (guidelines, policies, procedures, and laws) guide the authority and stakeholders in the conduct of health research in Liberia?
        i. Are these documents adequate?
            1. If no, what further regulations, in your experience, are needed to guarantee the ethical and legal conduct of health research?
    b. Is the LMHRA playing any direct role, when it comes to the following specific aspects of regulating health research:
        i. Reviewing
            1. Scientific
            2. Ethics
        ii. Approving
        iii. Monitoring
    c. If yes, what does this role involve:
        i. Reviewing
            1. Scientific
            2. Ethics
            3. Is said review independent of external institutional review?
            4. Is said review carried out in any particular order (say ethics review before scientific/LMHRA review or vice versa)?
        ii. Approving
        iii. Monitoring
    d. If no, do you think such functions are needed?
2) Is there a pre-defined process (es) that must be followed by a researcher/research institution in order to conduct acceptable health research, particularly involving human participants?
    a. Can you outline said process?
3) In your experience, what is the stance of Liberian ethical-legal frameworks on the below listed ethical issues:
    a. Insurance for research-related injury
    b. Post-trial access
    c. Ancillary care for research participants
    d. Community engagement/participation
    e. Standard of care
    f. Compensation for research participation
    g. Fair participant selection
        i. If they are not addressed by local regulations, how do you usually handle such issues?
4) In your experience, what legal safeguards are there against research misconduct/abuses?
    a. What needs to be done, if there are none?
5) What immediate plans does the LMHRA have, as it relates to regulating/approving/monitoring the ethical conduct of health research?
6) Is there anything else that we may not have covered that you may want to bring to my attention?

THANK YOU FOR YOUR TIME AND PARTICIPATION

8.6 Appendix 6: Interview Schedule for NPHIL

Thank you so much for agreeing to take part in this study, as a representative of the NPHIL. I am mainly interested in having a conversation with you on the governance of health research in Liberia, especially as it relates to the role of this newly established entity.

1) Does NPHIL have a role in the regulation of health research?
    a. If yes, which national documents (guidelines, policies, procedures, and laws) guide the institute and stakeholders in the conduct of health research in Liberia?
        i. Are these documents adequate?
            1. If no, what further regulations, in your experience, are needed to guarantee the ethical and legal conduct of health research?
    b. Is NPHIL playing any direct role, when it comes to the following specific aspects of regulating health research:
        i. Reviewing
            1. Scientific
            2. Ethics
        ii. Approving
        iii. Monitoring
    c. If yes, what does this role involve:
        i. Reviewing
            1. Scientific
            2. Ethics
            3. Is said review independent of external institutional review?
        ii. Approving
        iii. Monitoring
    d. If no, do you think such functions are needed?
2) Is there a pre-defined process (es) that must be followed by a researcher/research institution in order to conduct acceptable health research, particularly involving human participants?
    a. Can you outline said process?
3) In your experience, what legal safeguards are there against research misconduct/abuses?
    a. What needs to be done, if there are none?
4) What immediate plans does the Institute have, as it relates to regulating/approving/monitoring the ethical conduct of health research?
5). Is there anything else that you would like to mention?

THANK YOU FOR YOUR TIME AND PARTICIPATION

8.7 Appendix 7: Interview Schedule for Researchers

Thank you so much for agreeing to take part in this study. I am mainly interested in having a conversation with you on the governance of health research in Liberia, especially as it relates to getting the perspective of a researcher, whose activities are meant to be streamlined by whatever governance structures are in place.

1) Do you have any form of ethics training?
   (If 'Yes', Take note of the nature of training, e.g. formal degree or diploma training, Certificate Course, workshops, online self-taught, etc)

2) In your experience, which national documents (guidelines, policies, procedures, and laws) guide the conduct of health research in Liberia?
   a. Are these documents adequate?
      i. If no, what further regulations, in your experience, are needed to guarantee the ethical and legal conduct of health research?
3) In your experience, what is done when legal infractions (illicit drug use, child abuse, rape, etc.) are uncovered during research? Is there mandatory reporting?
   a. If not already required:
      i. Do you think there should be mandatory reporting?
      ii. How do you usually handle such cases?
4) In your experience, is there any post-approval monitoring by Ethics (ECs) or Regulatory (LMHRA/MoH/NPHIL) authorities?
   a. If yes, what is the frequency of such monitoring?
   b. If no, do you think such monitoring is needed?
5) What is the extent your relationship with local Research Ethics Committees?
   a. Which protocols do you submit for ethics approval, and do you make the determination by yourself?
   b. Is there a guide from the REC, when it comes to what to submit?
   c. Are these guides accessible?
   d. Are you satisfied with the review you get?
      i. Ethics review?
      ii. Scientific reviews?
   e. What changes, if any, are needed to improve the quality of:
      i. Ethics review?
      ii. Scientific reviews?
6) In your experience, what is the stance of the Liberian ethical-legal frameworks on the below listed ethical issues:
   a. Insurance for research-related injury
   b. Post-trial access
   c. Ancillary care for research participants
   d. Community engagement/participation
   e. Standard of care
   f. Compensation for research participation
   g. Fair participant selection
      i. If they are not addressed by local regulations, how do you usually handle such issues when designing or conducting studies?
7) What legal safeguards, if any, are there against research misconduct/abuses?
   a. What needs to be done, if there are none?
8) <u>Is there anything else that you would like to mention that we may not have covered?</u>

THANK YOU VERY MUCH FOR YOUR PARTICIPATION

8.8 Appendix 8: Document Assessment Framework

Principles	Benchmarks (Modified)
Collaborative Partnership	• Address research fairness (north-south partnerships)? • Encourage community involvement and synergic interactions with local authorities? • Require capacity building? • Require respect for and adherence to local laws? • Address fair sharing of benefits with participants?
Social Value	• Require that studies prioritize and address local health needs? • Ensure results publication/dissemination and utilization to strengthen local systems (policy)? • Prevent research weakening local health system?
Scientific Validity:	• Ensure research is conducted by academically and ethically qualified researchers? • Ensure methodological designs achieve outcomes? • Require prior knowledge?
Fair selection of study population	• Requirement for fair and equitable selection? • Provide clear definition of vulnerable populations? • Address the problem of under-representation (children, pregnant women)? • Ensure protections for vulnerable populations?
Favourable risk-benefit ratio	• Clearly Stated Requirement for risk-benefit ratio? • Provide clear definition for 'risk" and "benefit?' • Are there guidelines on handling research abuse or violations?
Independent review	• Mandate ethics review? • Are there recognized independent ECs? • Do they address conflicts of interests? • Prevention of "ethics shopping?" • Ensure post-approval monitoring? • Is there oversight of ECs?
Informed consent	• Is there a requirement for informed consent? • Provide clarity on consent/assent for those with limited agency? • Provide for the use of unwritten/unconventional consent? • Ensure use of local languages, where necessary?

Respect for recruited participants and study communities	• Guarantee protection of confidentiality/privacy? • Are there mandatory reporting obligations? • Ensure right refusal withdrawal with no penalty? • Require provision of periodic updates on studies? • Address post-trial access to final products? • Address the issue of ancillary care obligations? • Require the provision of treatment or insurance for trial-related injuries? • Procedure for resolving contentious findings?

Adaptation of the Emanuel et al (2004) framework

8.9 Appendix 9: Document Assessment Table

Emanuel et al Framework (modified)		Legal / Regulatory Frameworks							Ethical Frameworks	
Principles	**Benchmarks**	**Doc #1**	**Doc #2**	**Doc #3**	**Doc #4**	**Doc #5**	**Doc #6**	**Doc #7**	**Doc #1**	**Doc #2**
Collaborative Partnership	Address research fairness (north-south partnerships)?									
	Encourage community involvement and synergic interactions with local authorities?									
	Require capacity building?									
	Require respect for and adherence to local laws?									
	Address fair sharing of benefits with participants?									
Social Validity	Require that studies prioritize and address local health needs?									
	Ensure results publication/dissemination and utilization to strengthen local systems (policy)?									
	Prevent research weakening local health system?									
Scientific Validity:	Ensure research is conducted by academically and ethically qualified researchers?									
	Ensure methodological designs achieve outcomes?									
	Require prior knowledge?									
Fair selection of study population	Requirement for fair and equitable selection?									
	Provide clear definition of vulnerable populations?									

	Address the problem of under-representation (children, pregnant women)?									
	Ensure protections for vulnerable populations?									
Favourable risk-benefit ratio	Clearly Stated Requirement for risk-benefit ratio?									
	Provide clear definition for 'risk" and "benefit?'									
	Are there guidelines on handling research abuse or violations?									
Independent review	Mandate ethics review?									
	Are there recognized independent ECs?									
	Do they address conflicts of interests?									
	Prevention of "ethics shopping?"									
	Ensure post-approval monitoring?									
	Is there oversight of ECs?									
Informed consent	Is there a requirement for informed consent?									
	Provide clarity on consent/assent for those with limited agency?									
	Provide for the use of unwritten/unconventional consent?									
	Ensure use of local languages, where necessary?									
Respect for recruited participants and study communities	Guarantee protection of confidentiality/ privacy?									
	Are there mandatory reporting obligations?									
	Ensure right refusal withdrawal with no penalty?									
	Require provision of periodic updates on studies?									

Adaptation of the Emanuel et al (2004) framework

8.10 Appendix 10: Emanuel et al Benchmarks

Principles	Benchmarks
Collaborative Partnership	• Develop partnerships with researchers, makers of health policies, and the community. • Involve partners in sharing responsibilities for determining the importance of health problem, assessing the value of research, planning, conducting, and overseeing research, and integrating research into the health-care system. • Respect the community's values, culture, traditions, and social practices. • Develop the capacity for researchers, makers of health policies, and the community to become full and equal partners in the research enterprise. • Ensure that recruited participants and communities receive benefits from the conduct and results of research. • Share fairly financial and other rewards of the research.
Social Value	• Specify the beneficiaries of the research—who. • Assess the importance of the health problems being investigated and the prospective value of the research for each of the beneficiaries—what. • Enhance the value of the research for each of the beneficiaries through dissemination of knowledge, product development, long-term research collaboration, and/or health system improvements. • Prevent supplanting the extant health system infrastructure and services
Scientific Validity:	• Ensure that the scientific design of the research realizes social value for the primary beneficiaries of the research. • Ensure that the scientific design realizes the scientific objectives while guaranteeing research participants the health-care interventions to which they are entitled. • Ensure that the research study is feasible within the social, political, and cultural context or with sustainable improvements in the local health-care and physical infrastructure
Fair selection of study population	• Select the study population to ensure scientific validity of the research. • Select the study population to minimize the risks of the research and enhance other principles, especially collaborative partnership and social value. • Identify and protect vulnerable populations.
Favorable risk-benefit ratio	• Assess the potential risks and benefits of the research to the study population in the context of its health risks. • Assess the risk-benefit ratio by comparing the net risks of the research project with the potential benefits derived from collaborative partnership, social value, and respect for study populations.
Independent review	• Ensure public accountability through reviews mandated by laws and regulations. • Ensure public accountability through transparency and reviews by other international and nongovernmental bodies, as appropriate. • Ensure independence and competence of the reviews
Informed consent	• Involve the community in establishing recruitment procedures and incentives. • Disclose information in culturally and linguistically appropriate formats. • Implement supplementary community and familial consent procedures where culturally appropriate. • Obtain consent in culturally and linguistically appropriate formats. • Ensure the freedom to refuse or withdraw.
Respect for recruited participants and study communities	• Develop and implement procedures to protect the confidentiality of recruited and enrolled participants. • Ensure that participants know they can withdraw without penalty. • Provide enrolled participants with information that arises in the course of the research study. • Monitor and develop interventions for medical conditions, including research-related injuries, for enrolled participants, at least as good as existing local norms. • Inform participants and the study community of the results of the research.

8.11 Appendix 11: Summary of CIOMS Guidelines

Guideline	Summary
Guideline 1	• Deals with the Scientific and Social Value and Respect for rights, and it maintains that an ethical study should have both a scientific and social value. • It also requires that there is unfettered respect for the rights and welfare of individual participants and community. • It additionally requires that the studies are conducted by qualified investigators
Guideline 2	• Covers Research Conducted in Low-Resource Settings. • In this guideline, researchers are required to engage with the communities they will be working in to make sure that the research reflects the priorities of these communities. • It maintains that there must be plans to provide additional benefits like training, and ensure post-trial access to the products of the research.
Guideline 3	• Centred on Equitable Distribution of Benefits and Burdens. • Requires fair participant selection for research. It stresses that inclusion and exclusion criteria should not be discriminatory, and that under-represented populations should be given opportunities to participate.
Guideline 4	• Deals with Potential Risks and Benefits to Individuals. • It requires that there is adequate risk-benefit analysis before a study commences, and that measures must be put in place to minimize risks and maximize benefits for individuals and group or communities
Guideline 5	• Has to do with the Choice of Controls in Clinical Trials. • It maintains that the use of controls and placebos are permissible by ethics committees, but that there must be clear justification, minimization of risks, and appropriate arrangements for care.
Guideline 6	• Deals with Caring for Participant Health Needs. • Requires that researchers make plans to take care of the health needs of participants, like the provision of ancillary care
Guideline 7	• Is about Community Engagement, which requires that communities must be appropriately engaged at every step of the research process. • It maintains that failure to engage communities undermines the social value of research
Guideline 8	• Concerned with Collaborative Partnership and Capacity-building for Research and Ethics Review. • This guideline requires that where there is evident lack of capacity (research & ethics review), sponsors, and researchers have an ethical obligation to help develop them
Guideline 9 & Guideline 10	• Deal with Informed Consent and its Modifications and Waivers. • At the core of these guidelines is the requirement that informed consent is obtained from all capable participants, and that any modification or waiver of informed consent must be authorized by an ethics committee.
Guideline 11 & Guideline 12	• Deal with the Collection, Storage, and Use of Biological Materials/data and Health-related Research Data. • Maintain that when biological materials/data or other health-related data are collected from individuals, they remain extensions of those individuals. Therefore, all of the ethical requirements, like consent, still apply. • If said materials or data are to be used for future purposes, the consent must be broad enough to cover such use, or an ethics committee must approve
Guideline 13 & Guideline 14	• Deal with Reimbursement/Compensation for participation and Treatment/Compensation for related harm.

	• These requirements maintain that participants in research must be justly reimbursed or compensated (as determined by ethics committees) for participation, without necessarily being seen as undue inducement. • Additionally, there must be plans to treat or compensate participants for research-related harms or injuries.
Guidelines 15, 16, 17, 18, & 19	• Concerned with Vulnerable Individuals or Groups of Concern (incapacitated adults, children, pregnant women, etc.). • The general spirit of these guidelines is that such individuals or groups must be included in research, except where there is justifiable reason to exclude them. • However, because of their peculiar situations, ethics committees must ensure that adequate protections are in place; these individuals must still give an assent (if possible) and consent of a legal representative must be obtained
Guideline 20	• Addresses Research in Disasters or Disease Outbreaks. • This guideline insists that despite the logistical and ethical hurdles in such situations (consent under duress, difficulty of ethics review, use of unproven drugs), everything must be done to comply with the stipulations of this document.
Guideline 21	• Addresses the issue of using Cluster Randomized Trials (CRT). • In a study using CRT, stakeholders, including ethics committees, must ensure some conditions like a clear understanding of who the actual participants are, a determination as to whether informed consent is required or feasible, or whether gatekeeper permissions are required.
Guideline 22	• Related to Data obtained electronically (Online or Digital). • This guideline maintains that using these means of collecting data doesn't absolve the researcher of responsibility to protect the privacy and confidentiality of individuals.
Guideline 23	• Pertains to Requirement for establishing IRBs and their Functions. • The crux of this requirement is that all research that involve human subjects must be submitted to, and approved by an appropriately constituted IRB. • Where there is no IRB, stakeholders must establish and enable them. IRBs are encouraged to foster communication between themselves
Guideline 24	• Deals with Public Accountability of Research. • This guideline obliges researchers to have their studies registered, and also ensure that findings from their studies, whether positive or negative, are published or made available
Guideline 25	• It mandates that stakeholders in the research enterprise must assess, declare, and take steps to mitigate conflicts of interest situations that apply to their work.

8.12 Appendix 12: Highlights of 45 CFR 46

Subpart	Summary
Subpart A	• Technically the "Common Rule," is referred is as Basic Policy. • It outlines the scope of the policy; includes basic definitions of relevant terms (like research and minimal risk); covers compliance with the policy; discusses institutional review boards (IRBs), including their membership, functions, and processes, amongst others.
Subpart B	• Centred on Additional Protections for pregnant women, human foetuses, and neonates, if they are to be involved in research. • It clearly spells out the requirements for conducting research involving this group, and the special protections that they need. • According to this section, on the critical issue of consent, only the pregnant woman can consent, in case the study is beneficial for only her, for both she and the fetus, or none of them. • However, if the benefit is only for the fetus, the father's consent is also needed, except if he's not available. • In the case of a viable neonate, subparts A and D are utilized. • For a nonviable neonate, both parents must give consent, except if one is unavailable. • A similar situation obtains in case of a neonate of uncertain viability, though actions should be geared towards improving viability. • The decision regarding viability or the lack of it cannot be left to the research team
Subpart C	• About Additional Protections Prisoners, when involving them in biomedical or behavioural research. • It is meant to guarantee their rights to participate in research, but also ensure that they do so willing. • Such research also have to be about something that relates to their status as prisoners, or a condition that affects them disproportionately.
Subpart D	• Deals with Additional Protections for Children in research. • This part addresses the prerequisite conditions for involving children in research, and the special protections that should be accorded them, especially bearing in mind that they lack the autonomy needed to make informed decisions. • It requires an assent from children, and the consent of a legally authorized representative. • Additionally, such studies must be beneficial to them or to other children.
Subpart E	• Added in 2009, deals with the administrative processes of IRB Registration. • It might not be directly tied to the protection of human subjects, but given the crucial role played by IRBs, it is also a significant part of the regulations

8.13 Appendix 13: Key Responses of Stakeholders

Issue		Oversight Entities					Researchers					
		Entity 1 Rep	Entity 2 Rep	Entity 3 Rep	Entity 4 Rep	Entity 5 Rep	**R1**	**R2**	**R3**	**R4**	**R5**	**R6**
In content, are Documents Adequate?		NO	NO	NO	NO	YES	Not sure	NO	NO	NO	NO	NO
What's needed?		Localize Principles, Awareness creation, & Detailed Guidelines	Detailed Guidelines	Detailed Guidelines	Detailed Guidelines	Structural Organization	Stringent Regulations & Capacity building	Stringent Regulations & Structural Organization	Detailed Guidelines	Implementation, Detailed Guidelines, & Structural Organization	Detailed Guidelines & Structural Organization	Structural Organization & Prioritization
Perform/aware of Post-approval monitoring?	**Active**	NO	NO	YES	NO	NO	NO	YES	NO	NO	NO	NO
	Passive	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES
	Active Needed?	YES	YES	___	YES	YES	YES	___	YES	YES	YES	YES
Oversight body for ECs/Research	**Present?**	NO	NO	___	NO	NO	___	___	___	___	___	___
	If not, needed?	YES	YES	___	YES	YES	___	___	___	___	___	___
Detailed local guidance on key ethical issues	**Present?**	NO	NO	NO	___	YES	NO	NO	NO	NO	NO	NO
	If not, needed?	YES	YES	YES		___	YES	YES	YES	YES	YES	YES
	Exist?	NO	NO	Yes	NO	Yes	Not sure	Not sure	Yes	Not sure	No	No

Guidelines on abuse?	**If not, needed?**	YES	YES	___	YES	___	Yes	Yes	Yes	Yes	Yes	Yes
Mandatory Reporting	**Aware of any?**	NO	NO	___	___	Yes	Not sure	No	No	No	No	No
	If not, needed?	NO	YES	___	___	___	Not sure	Yes	Yes	Yes	Yes	Yes
Training	**Any?**	___	___	___	___	___	Yes	Yes	Yes	Yes	Yes	Yes
	Type	___	___	___	___	___	GCP Short course	Certificate, GCP	Certificate	GCP	NIH Online	Online, Workshops
Relation with ECs		___	___	___	___	___	Good	___	___	Good	Professional	Professional
Protocols	**Which submitted?**	___	___	___	___	___	Human Participants	Human Participant	___	Human Participant	___	All types
	Whose decision?	___	___	___	___	___	Ethics Committee	___	___	Ethics Committee	Self	Ethics Committee
Ethics Committee (EC) SOP	**Present?**	___	___	___	___	___	Not aware	___	Yes	Yes	Yes	Yes
	Accessible?	___	___	___	___	___	___	___	Yes	___	Yes	___
Satisfied with Reviews?		___	___	___	___	___	Yes	___	No	No	No	No
Suggestions for Ethics Committees		___	___	___	___	___	Better Communication	Composition, Better communication	Capacity building, Better communication, & Proper structuring	Composition, Detailed Guidelines	Composition, Capacity building	Independence, Capacity building, Detailed Guidelines
Aware of Ethics Review among early career researchers?		___	___	___	___	___	Relatively low	Not sure	Not optimal	Relatively low	Very little	Not at all
1: Public health law (PHL); 2: NREB Guidelines (NREB); 3: UL-PIRE IRB Handbook (UL-PIRE); 4: Clinical Trial Guidelines (CTG); 5: Research for Health Policy (RHP); 6: Constitution of Liberia (CoL); 7: National Health Policy (NHP)												

8.14 Appendix 14: Completed Document Assessment Table

Emanuel et al Framework (modified)		(Pertinent) Regulatory Frameworks of Liberia													Ethical Frameworks	
			MGCSP		LMHRA			MoH/NPHIL								
Principle	**Benchmarks**	**Consti-tution**	**Child-ren's Law**	**Child Welfare Policy**	**Clinical Trial Guideline**	**ACT**	**Penal Code**	**Research Policy**	**Health Policy & Plan**	**NPHIL ACT**	**Public Health Law**	**Health Communi-cation Strategy**	**Human Rights Act**	**LISGIS Act**	**NREB**	**UL-PIRE IRB**
Collaborative Partnership	Address research fairness (north-south partnerships)?							X								
	Encourage community involvement and synergic interactions with local authorities?					X		X	X		X	X				
	Require capacity building?				X			X								
	Require respect for and adherence to local laws?							X								
	Address fair sharing of benefits with participants?															
Social Value	Require that studies prioritize and address local health needs?							X								
	Ensure results publication/dissemination and utilization to strengthen local systems (policy)?				X			X								X
	Prevent research weakening local health system?							X								

Scientific Validity	Ensure research is conducted by academically and ethically qualified researchers?				X						X			X	X	X
	Ensure methodological designs achieve outcomes?				X			X							X	X
	Require prior knowledge?				X			X								X
Fair selection of study population	Requirement for fair and equitable selection?				X			X							X	X
	Provide clear definition of vulnerable populations?		X		X											X
	Address the problem of under-representation (children, pregnant women)?															
	Ensure protections for vulnerable populations?		X	X				X								X
Favourable risk-benefit ratio	Clearly Stated Requirement for risk-benefit ratio?				X			X							X	X
	Provide clear definition for 'risk" and "benefit?'							X								X
	Are there guidelines on handling research abuse or violations?					X			X		X		X		X	X
Independent review	Mandate ethics review?				X			X	X						X	X
	Are there recognized independent ECs?							X								
	Do they address conflicts of interests?				X			X							X	X
	Prevention of "ethics shopping?"							X								

	Ensure post-approval monitoring?				X			X							X	X
	Is there oversight of ECs?															
Informed consent	Is there a requirement for informed consent?	X			X			X			X				X	X
	Provide clarity on consent/assent for those with limited agency?		X	X							X					X
	Provide for the use of unwritten/unconventional consent?															X
	Ensure use of local languages, where necessary?															
Respect for recruited participants and study communities	Guarantee protection of confidentiality/privacy?	X	X		X		X	X		X	X			X	X	X
	Are there mandatory reporting obligations?		X				X				X					
	Ensure right refusal withdrawal with no penalty?				X											X
	Require provision of periodic updates on studies?															X
	Address post-trial access to final products?															
	Address the issue of ancillary care obligations?															
	Require the provision of treatment or insurance for trial-related injuries?				X			X								X
	Procedure for resolving contentious findings?															

8.15 Appendix 15: Respondents Awareness of major local Documents

Interviewee(s)		Local Documents Cited by Respondents	Part of major 5 identified pre-interview?	# of Major 5 cited	% of Major 5 cited	% Average/Group	Overall % Average
Oversight Entities	Entity #1 Rep	UL-PIRE IRB Handbook	Yes	1	20%	52%	64%
	Entity #2 Rep	Public Health Law	Yes	2	40%		
		NREB Guideline	Yes				
	Entity #3 Rep	Clinical Trial Guideline	Yes	2	40%		
		Public Health Law	Yes				
	Entity #4 Rep	Research for Health Policy	Yes	4	80%		
		Public Health Law	Yes				
		UL-PIRE IRB Handbook	Yes				
		NREB Guideline	Yes				
	Entity #5 Rep	Research for Health Policy	Yes	4	80%		
		UL-PIRE IRB Handbook	Yes				
		National Health Policy & Plan	No				
		Clinical Trial Guideline	Yes				
		NREB Guideline	Yes				
Researchers	R 1	Constitution of Liberia	No	3	60%	73%	
		Clinical Trial Guideline	Yes				
		NREB Guideline	Yes				
		UL-PIRE IRB Handbook	Yes				
	R 2	Clinical Trial Guideline	Yes	4	80%		
		NREB Guideline	Yes				
		UL-PIRE IRB Handbook	Yes				
		Research for Health Policy	Yes				
	R 3	Research for Health Policy	Yes	3	60%		
		NREB Guideline	Yes				
		UL-PIRE IRB Handbook	Yes				

	R 4	NREB Guideline	Yes	3	60%		
		UL-PIRE IRB Handbook	Yes				
		Public Health Law	Yes				
	R 5	Research for Health Policy	Yes	4	80%		
		Public Health Law	Yes				
		NREB Guideline	Yes				
		UL-PIRE IRB Handbook	Yes				
	R 6	Research for Health Policy	Yes	5	100%		
		NREB Guideline	Yes				
		UL-PIRE IRB Handbook	Yes				
		Public Health Law	Yes				
		Clinical Trial Guideline	Yes				

8.16 Appendix 16: Proposed Research Governance Framework (Description)

Stage of Frame work	Descriptive Highlights
Gate-keeper Permission	• At the pinnacle of this proposed governance framework is the government of Liberia, through the Ministry of Health. This level also includes other relevant ministries and agencies of government, vis a vis the research issue under consideration. For example the gate-keeper permission for a research dealing with children and other vulnerable groups might also need some sort of endorsement from the Gender Ministry; or one with Public Health Implication might need endorsement from the National Public Health Institute of Liberia (NPHIL). • For research being done at academic institutions, such administrative or institutional level acceptance will be provided by the local academic institution (departments, colleges, or university level) and that of county or district level representation of pertinent government entities. • The acceptance gotten from this phase is in no way the ultimate go-ahead needed for the conduct of health research, especially those involving human participants (this will come in the next level). • It is to ensure relevance of the study to the local research and development agenda of the country, facilitate the tracking of such research (like the national database supposedly held at the MoH), and to help with some degree of initial guidance.
Regulatory & Ethical Approval	• For regulatory go-ahead, researchers must apply to and receive approvals from the National Health Research Council (NHRC) and Liberia Medicines and Health Products Regulatory Authority (LMHRA) (clinical trials). For other studies including observational and epidemiological ones regulatory is only required from the NHRC. For ethical approval, depending on the type of research being carried out, it must be received from either the NREB (clinical trials) or the UL-PIRE IRB or any other properly recognized ethics committee. Submissions to the ethics committees must include relevant gate-keeper permissions, and in the case of international studies, ethics approval from the other country (ies) concerned. • Though receiving ethical and regulatory approval for a study allows a researcher to proceed with his/her study, this approval is no means the end of the interaction between the study team and these authorities. As per convention, these institutions, for continuous oversight purposes, usually require regular reports and updates, and can even make site visits to ascertain that the terms of the approved protocols are being adhered to.
Implementation	• Once a research project or study has received gate-keeper permission, along with regulatory and ethical approvals, the study team can proceed to activating the study. • Most of the activities at this phase fall within the purview of the researcher or research institution. However, as alluded to earlier, the conduct of the research

	must be within the confines of set terms, as approved by the regulatory and ethics authorities, both locally and internationally, as the case may be. One way these institutions ensure said compliance is by requiring the conductors of research to make regular reports, at specified intervals, as it relates to status of the approved studies and the occurrence of events that might pose a risk, however apparently minimal it turns out to be. These authorities also reserve the right to make on-site visits to find out, for themselves, if these terms are being complied with. • In this regard, governance at this level mainly has to do with the appropriate and timeous filing of said reports, coupled with on-site visitations. Whatever reporting requirements that have been agreed to by researchers must be adhered to, and the research governance institutions must also follow through on their responsibility to complement these reports by carrying out active monitoring of these research facilities and documents. • The relationship at this level also includes timely sharing of critical pieces of information, which can include seeking clarifications on what needs to be done, if there exists any doubts, and also adequate dissemination, through appropriate channels, of information that might have policy or safety significance, i.e. incidental findings.
Publication or Dissemination of Results (Output)	• This phase kicks in at the conclusion of the study. Again, local ethics committees and the LMHRA (for clinical trials) have some end of study reporting requirements that must be followed to the letter. As specified in their guidelines, these different reports, taking into account study type and duration, must be made according to particular timelines. They also require that study participants are informed about the findings of the study). • Besides these ethics and regulatory authorities, the government of Liberia also requires that, for the purposes of policy formulation, policy and systems strengthening, and serving as future reference, findings, as stated in section 2.4 of the 2018 RHP, must be shared with the Ministry. • The dissemination of research results must also carefully take into concern the views of the participants and participant communities. One practice that has been practiced elsewhere is that of having a mechanism whereby a representative group of participants or participant communities and that of researchers can amicably resolve issues surrounding contested findings in a way that doesn't elicit mistrust and, consequently forestall future research. These researcher-community engagements should either harmonize the issue or make sure that both sides are adequately represented in the final output.

8.17 Appendix 17: Ministry of Health Permission

REPUBLIC OF LIBERIA

MINISTRY OF HEALTH & SOCIAL WELFARE

P. O. BOX 10 – 9009
1000 MONROVIA 10, LIBERIA
WEST AFRICA

Research Unit
Department of Planning
Ministry of Health
Liberia

February 5, 2018

Kokulo Franklin
Partnership for Research on Ebola Virus in Liberia
1st Floor, JFK Compound,
22nd Street, Sinkor,
Monrovia, Liberia

RE: Approval to Investigate a Study Entitled: A Forensic Review and Evaluation of the Regulatory and Ethical Framework Governing Health-Related Research in Post-Ebola Liberia."

Dear Mr. Kokulo,

As per your request for study approval sent to the Ministry of Health on December 18, 2017, I write to inform you that you have been granted an approval to conduct the study entitled: ***A Forensic Review and Evaluation of the Regulatory and Ethical Framework Governing Health-Related Research in Post-Ebola Liberia."***

This approval letter, however, cannot be used in place of an ethical clearance as such you are kindly advised to submit your study protocol for ethical approval. Additionally, the Ministry of Health will appreciate if you could share with us upon completion of your study the findings for future reference.

Sincerely yours, [redacted]

Nelson K. Dunbar
Research Director

8.18 Appendix 18: LMHRA Permission

LIBERIA MEDICINES & HEALTH PRODUCTS REGULATORY AUTHORITY (LMHRA)
P.O.Box 1994, VP Road, Old Road, Oldest Congo Town
Monrovia, Liberia
LMHRA

March 16, 2018

Mr. Kokulo Franklin
Partnership for Research on Ebola Virus in Liberia
1st Floor,
JFK Compound,
22nd Street, Sinkor,
Monrovia, Liberia

Dear Mr. Franklin:

Gate-keeper Permission

I am writing to acknowledge your request for "gate-keeper" permission from the Liberia Medicines and Health Products Regulatory Authority (LMHRA), and to inform you that the LMHRA is opened to working along with you, to the extent possible, in order to carry out your study entitled: "A Forensic Review of the Regulatory and Ethical Framework Governing Health-Related Research in Post-Ebola Liberia."

This permission, however, does not in any way guarantee participation, as that will depend on whether or not you manage to obtain ethics approval from a duly constituted research ethics committee (s), as well as the informed consent of the "contact person" that will be asked to participate, on behalf of the Institute, in the interview.

You are welcome to engage the Liberia Medicines and Health Products Regulatory Authority (LMHRA), if you have any further requests or concerns.

Best Regards.

Very truly yours,

[redacted]

Joseph M. Redd, Sr.
Human Resources Manager
Acting Managing Director/LMHRA
Email: wisemanchampredd@gmail.com

8.19 Appendix 19: NPHIL Permission

National Public Health Institute Of Liberia

Preventing and Controlling Public Health Threats

Office of the Deputy Director General
for Technical Services

Ref. No: NPHIL/RL/MPF-DDGT/027/'18

February 19, 2018

Mr. Kokulo Franklin
Partnership for Research on Ebola Virus in Liberia
1st Floor,
JFK Compound,
22nd Street, Sinkor,
Monrovia, Liberia

Dear Mr. Franklin:

Gate-keeper Permission

I am writing to acknowledge your request for "gate-keeper" permission from the National Public Health Institute of Liberia, and to inform you that the Institute is opened to working along with you, to the extent possible, in order to carry out your study entitled "A Forensic Review of the Regulatory and Ethical Framework Governing Health-Related Research in Post-Ebola Liberia."

This permission, however, does not in any way guarantee participation, as that will depend on whether or not you manage to obtain ethics approval from a duly constituted research ethics committee (s), as well as the informed consent of the "contact person" that will be asked to participate, on behalf of the Institute, in the interview.

You are welcome to engage the Institute, if you have any further requests or concerns.

Best regards,

[redacted]

Mosoka P. Fallah, PhD, MPH, MA

P.O. Box 1871, Emergency Operations Center, Congo Town Back Road, 1000 Monrovia, 10 Liberia

8.20 Appendix 20: UL-PIRE IRB Permission

UNIVERSITY OF LIBERIA
CAPITOL HILL
MONROVIA, LIBERIA
WEST AFRICA

Office of the Institution Review Board

IORG0004203
Federal Wide Assurance#: FWA00004982

February 16, 2018

Mr. Kokulo Franklin
Partnership for Research on Ebola Virus in Liberia
1st Floor,
JFK Compound,
22nd Street, Sinkor,
Monrovia, Liberia

Dear Mr. Franklin:

Gate-keeper Permission

I am writing to acknowledge your request for "gate-keeper" permission from the **UL-PIRE IRB**, and to inform you that the **UL-PIRE IRB** is opened to working along with you, to the extent possible, in order to carry out your study entitled **"A Forensic Review of the Regulatory and Ethical Framework Governing Health-Related Research in Post-Ebola Liberia".**

This permission, however, does not in any way guarantee participation, as that will depend on whether or not you manage to obtain ethics approval from a duly constituted research ethics committee (s), as well as the informed consent of the "contact person" that will be asked to participate, on behalf of the Institute, in the interview.

You are welcome to engage the **UL-PIRE IRB**, if you have any further requests or concerns.

Sincerely yours,

[redacted]

Ms. Cecelia A. Morris, MSN
Chairperson, UL-PIRE-IRB

E-mail: morris.caletha@gmail.com | tegli@ul-pireafrica.org Phone #: 0886-522-833 | 0886-583-774

8.21 Appendix 21: BREC Approval

UNIVERSITY OF KWAZULU-NATAL
INYUVESI YAKWAZULU-NATALI

31 July 2018

Mr K Franklin (217075678)
School of Applied Human Sciences
College of Humanities
Franklinkok.80@gmail.com

Dear Mr Franklin

Protocol: A forensic review and evaluation of the regulatory and ethical framework governing health-related research in post-Ebola Liberia.
Degree: M.Soc **BREC Ref No: BE401/18**

EXPEDITED APPLICATION: APPROVAL LETTER

A sub-committee of the Biomedical Research Ethics Committee has considered and noted your application received on 11 July 2018.

The conditions have been met and the study is given **full ethics approval** and may begin as from 31 July 2018. Please ensure that site permissions are obtained and forwarded to BREC for approval before commencing research at a site.

This approval is valid for one year from **31 July 2018.** To ensure uninterrupted approval of this study beyond the approval expiry date, an application for recertification must be submitted to BREC on the appropriate BREC form 2-3 months before the expiry date.

Any amendments to this study, unless urgently required to ensure safety of participants, must be approved by BREC prior to implementation.

Your acceptance of this approval denotes your compliance with South African National Research Ethics Guidelines (2015), South African National Good Clinical Practice Guidelines (2006) (if applicable) and with UKZN BREC ethics requirements as contained in the UKZN BREC Terms of Reference and Standard Operating Procedures, all available at http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx.

BREC is registered with the South African National Health Research Ethics Council (REC-290408-009). BREC has US Office for Human Research Protections (OHRP) Federal-wide Assurance (FWA 678).

The sub-committee's decision will be noted by a full Committee at its next meeting taking place on **14 August 2018.**

We wish you well with this study. We would appreciate receiving copies of all publications arising out of this study.

Yours sincerely

[redacted]

Prof D Wassenaar
Deputy Chair: Biomedical Research Ethics Committee

Supervisor: mkhize@ukzn.ac.za

Biomedical Research Ethics Committee
Professor V Rambiritch (Chair)
Westville Campus, Govan Mbeki Building
Postal Address: Private Bag X54001, Durban 4000
Telephone: +27 (0) 31 260 2486 **Facsimile:** +27 (0) 31 260 4609 **Email:** brec@ukzn.ac.za
Website: http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx

1910 - 2010
100 YEARS OF ACADEMIC EXCELLENCE

8.22 Appendix 22: UL-PIRE IRB Approval

UNIVERSITY OF LIBERIA
CAPITOL HILL
MONROVIA, LIBERIA
WEST AFRICA
Office of the Institution Review Board
IORG0004203

Certification of Human Approvals

August 21, 2018

Mr Kokulo Franklin
Partnership for Research on Ebola Virus in Liberia, 1st Floor, JFK Compound, 22nd Street, Sinkor, Monrovia
Email: k_frank1980@yahoo.com | franklinkok.80@gmail.com

Protocol Title: A Forensic Review and Evaluation of the Regulatory and Ethical Framework Governing Health-Related Research in Post Ebola Liberia

Protocol #: 18-08-122

Dear Mr. Franklin:

In accordance with 45 CFR 46, the human subjects protocol of the above referenced research study reviewed, as an initial expedited review on August 16, 2018 has been approved by the University of Liberia-Pacific Institute for Research & Evaluation Institutional Review Board (UL-PIRE IRB). This IRB will review the protocol during the implementation of the study to confirm human subject procedures. The expiration date of this approval is August 20, 2019 at Midnight.

Proposed changes to approved human subject research protocol must be reported promptly to the IRB to be reviewed and approved prospectively utilizing a continuing review application. No changes may be initiated without prior approval by the IRB, except where necessary to eliminate apparent immediate hazards to subjects. Any unanticipated problems involving risks to participants or others must be submitted promptly to the UL-PIRE IRB.

The IRB will require you to submit a progress report during the implementation of this study.
This institution is in compliance with requirements for protection of human subjects, including 45 CFR 46, 21 CFR 50, and 56, and 38 CFR16.

Kind regards.

Sincerely yours,

[redacted]

Ms. Cecelia A. Morris, MSN
Chairperson, UL-PIRE IRB

UL-PIRE IRB MONROVIA, LIBERIA

IRB Review Date: 08/16/2018
Approval Period: 08/21/2018 through 08/20/2019
Review Type: EXPEDITED/INITIAL
IRB Review Action: APPROVED
Assurance # FWA00004982

E-mail: morris.caletha@gmail.com | tegil@ul-pireafrica.org Phone #: 0886-522-833 | 0886-583-774